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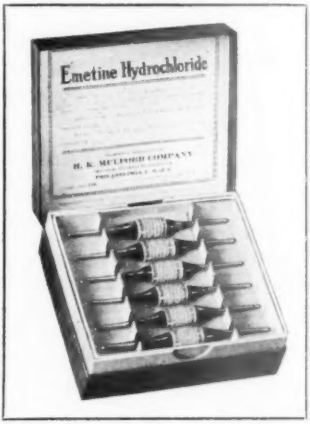

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* New York Medical Journal, July 4, 1914.
† A preliminary report read before the meeting of the Penna. Dental Asso., June 30, 1914

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THE

AMERICAN JOURNAL

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AUGUST, 1914

ORIGINAL ARTICLES

SYPHILIS OF THE LIVER, IMITATING CIRRHOSIS.[1]

By William Fitch Cheney, M.D.,

CLINICAL PROFESSOR OF MEDICINE, MEDICAL DEPARTMENT OF STANFORD UNIVERSITY, SAN FRANCISCO, CALIFORNIA.

That syphilis frequently affects the liver has been known for several centuries, but no one realized how frequently until quite recent times. The Wassermann reaction in the blood has taught us the meaning of many visceral lesions whose causation was formerly obscure: some of those in heart and aorta, for example, as well as in lungs, kidneys, and brain. So with the liver, manifestations of many different types of disease are now recognized to be due to syphilitic infection, and conditions formerly considered hopeless, because there was no way known to overcome them, are now occasionally combated successfully by attacking the disease that underlies them. Rolleston in his text-book on *Diseases of the Liver* describes seven different groups of cases which syphilis of the liver may simulate: (1) portal cirrhosis; (2) lardaceous disease; (3) tumor of the liver; (4) hepatic suppuration; (5) cholelithiasis; (6) splenic anemia; (7) hypertrophic biliary cirrhosis. Among these the largest group is that imitating cirrhosis, and it is surprising how often in a case corresponding in every clinical detail to portal cirrhosis, either hypertrophic or atrophic, a positive Wassermann reaction is found and improvement and even cure follow specific treatment. A group of such remarkable instances has come under the writer's observation during the past year, partly in the medical wards of the Stanford University Medical Department and partly

[1] Read before the San Joaquin County Medical Society, October 31, 1913.

in private work and these have prompted the decision to call attention to this subject.

CASE I.—A woman, aged forty-five years, entered the gynecological service in Lane Hospital, October 19, 1912, complaining that she had a tumor in the abdomen, which she had discovered only three weeks before. She had always previously been well, and now had no pain or discomfort except that in the abdomen. Examination showed a moderate amount of free fluid present in the peritoneal cavity, and a hard tumor in the lower abdomen, reaching as high as the navel. At operation about a gallon of clear fluid was evacuated, and the tumor, which proved to be a uterine fibroid, was removed. But it was also discovered that the gall-bladder contained gall-stones, the liver was hard and nodular, and there were numerous indurated glands in the retroperitoneal space. A piece of the nodular liver was removed for microscopic examination, and the pathologist's report on the sections read "syphilitic cirrhosis of the liver." The case was then transferred to the medical service.

The clinical feature of importance in this case was recurring ascites. Subsequent to the original removal of fluid by laparotomy, the abdomen refilled rapidly, so that three weeks later it had to be tapped and 3150 c.c. were removed. Ten days later 5400 c.c. more were withdrawn; after that the ascites never again became so excessive as to demand paracentesis. The right pleura, however, likewise gradually became filled with fluid, so that one month after the laparotomy this side of the chest had to be tapped, when 1500 c.c. were removed. One week later 1000 c.c. more were withdrawn, and only four days after that 1500 c.c. again; in each instance the aspiration of the chest was urgently required to relieve dyspnea. Always after the abdominal tapping a hard, irregular, tender mass could be felt in the right side of the abdomen, below the costal margin.

Besides the original report of the pathologist on the piece of liver tissue removed, not only the blood showed a triple X Wassermann reaction, but also the ascitic fluid and the pleural fluid when these were obtained. The combination of enlarged, nodular liver, with ascites, secondary involvement of the right pleural cavity, and such positive reactions in blood and peritoneal and pleuritic contents would have made the diagnosis sufficiently clear even without the pathologist's report.

This patient was given vigorous specific treatment. She received salvarsan intravenously in full dosage (0.6 gram) on October 27, and December 15; mercurial inunctions, 1 dram each day for thirty days, and potassium iodide in doses gradually increased from 10 grains up to 1 dram three times a day throughout her illness. But in spite of this she steadily grew weaker and thinner, and died on December 26. The autopsy showed syphilitic cirrhosis

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of the liver, syphiloma at the base of the liver, and syphilitic atheroma of the aorta.

The points of special interest in this case were (1) the insidiousness of onset. The patient must have had extensive changes in her liver long before she came for advice, but never realized that she needed treatment until warned by the discovery of a tumor in her abdomen, which after all was not the real disease. (2) The finding of a hard pelvic tumor associated with ascites naturally made the surgeon think first of cancer, and when the liver was found at operation to be likewise hardened and irregular, it was supposed to be involved by metastatic growth. This possibility of malignant disease can never be overlooked when a nodular liver and ascites are combined. (3) The occurrence of right-sided hydrothorax with ascites was formerly considered almost diagnostic of tuberculosis of peritoneum and pleura, but, as Cabot has shown, this pleuritic involvement may occur secondary to ascites from any cause, even from ordinary portal cirrhosis. (4) The failure of all treatment to save this patient's life was easily understood at autopsy, when the marked changes in liver structure lay revealed, for the killing of spirochetes and checking of further ravages could not avail to restore to usefulness a vital organ already so far destroyed. But all cases have not gone so far when first discovered, and for such there still is hope, as the following will show:

Case II.—A woman, aged forty-five years, entered the medical ward in Lane Hospital, February 13, 1913, complaining of "stomach troubles." Her general health had always been good, and she never had had any previous disease of any kind. She had been pregnant four times during her married life, but the first three had each time miscarried at seven months; the fourth pregnancy she had carried through successfully to full term, and the child was living and well. She began to ail just before Thanksgiving, 1912, with a great craving for food and water. Then she noted the following succession of symptoms: (1) Pain in the region of the navel and general abdominal distress after eating; this pain was slight and did not radiate; there was a sensation of a lump present about the navel, but she could discover none; the bowels became constipated. (2) A week or ten days after onset of these symptoms the skin became yellow, the urine dark, and the feces light colored; this jaundice persisted about a week, disappearing gradually just before Christmas. (3) She noticed about Christmas that she was losing weight rapidly, though her appetite remained good, and this combination of persistent loss of weight with good appetite had continued. (4) About January 1 she had an attack of vomiting, and noticed a small amount of blood in the vomitus; again during the night of January 30 she vomited about a pint of bright red fluid resembling blood, and the next day her stools contained dark red blood, and after that persistently resembled

tar in color and consistence. (5) Craving for food and persistent thirst had been present from the onset, so that she ate and drank large quantities, but nevertheless steadily lost in weight. The cardinal symptoms of her complaint were thus an attack of acute indigestion at the beginning, jaundice, loss of weight, hematemesis and melena, polyphagia, and polydipsia.

The woman was pale and poorly nourished. Neither the lungs, heart, nor arteries showed disease. The liver area was decreased to 8 cm.; the spleen increased to 12 cm., and the lower edge was palpable. While under observation in the ward she gradually developed marked ascites, though never excessive enough to demand tapping. The blood showed a decided secondary anemia. The urine showed a high specific gravity, and the constant presence of sugar, amounting to from 5 to 8 per cent. Finally, there was a positive triple X Wassermann reaction in the blood. The atrophic liver, enlarged spleen, ascites, with a previous history of indigestion and hematemesis, spoke clearly for hepatic cirrhosis, while the glycosuria, with polyphagia, polydipsia, and loss of weight might be explained by coincident disease of the pancreas, but both probably were luetic in origin. On treatment by salvarsan intravenously, mercury by inunction, and iodide of potassium internally in large doses she gradually improved greatly, the ascites almost entirely disappeared, and when last seen in May, 1913, though still far from well, she was able to get about all the time and to attend to her household duties.

While the foregoing cases were undoubtedly cirrhosis of the liver, but a special form of cirrhosis due to syphilis, it must be remembered that not all conditions resembling by clinical and by laboratory tests those described are necessarily cirrhosis or due to lues. The old observation that in clinical medicine two and two do not always make four is demonstrated by the following history:

Case III.—A man, aged fifty-five years, entered the medical ward on March 18, 1912, complaining of jaundice that had existed since the previous January. He had never been ill before. The present trouble began with severe diarrhea, persisting for a week, followed by slight jaundice, which rapidly deepened. He had since been given a limited diet, and to this attributed the fact that he had lost twenty pounds in weight. He had no subjective symptoms whatever. His appetite was good; digestion undisturbed; there was no pain in the abdomen or elsewhere, and no marked loss of strength. Examination showed extreme jaundice; a large, hard, smooth liver, measuring 13 cm. in area in the nipple line, and palpable for 8 cm. below the costal margin, with the lower border sharply defined; and an enlarged spleen with lower border palpable below the left costal margin. The liver was not particularly tender and not nodular. No other physical abnormalities were found, in the remainder of the abdomen or the rectum, to account for the jaundice.

The blood showed a triple X Wassermann reaction and combining this with the clinical history and physical findings a diagnosis was reached of syphilis of the liver. He was therefore given salvarsan intravenously on two different occasions, with an interval of two weeks between doses, followed by a course of mercurial inunction and by potassium iodide internally. But this treatment had no effect whatever upon his jaundice or upon the size of his liver or spleen. On the contrary, he steadily grew weaker, and ascites gradually developed. Therefore, on April 24 an exploratory laparotomy was done by Dr. Stillman, and this revealed at the upper border of the left lobe of the liver a hard, nodular mass as large as a man's fist. As this was considered inoperable, the abdomen was closed at once, but the patient died a few days later, on April 27. The autopsy disclosed a huge carcinoma of the liver, with central degeneration. No primary focus could be found elsewhere, after careful search, and the case was set down as one of primary hepatic carcinoma.

It seems probable that there was no relation whatever between this patient's real disease and his Wassermann reaction. The latter was undoubtedly evidence of syphilitic infection, but it did not give any reliable clue as to the nature of the pathological process in the liver; the two conditions were present simply by coincidence and not at all as cause and effect. It is possible, of course, that ordinary portal cirrhosis and a Wassermann reaction may in the same way coexist in a patient without meaning that the cirrhosis is luetic; but when a marked beneficial effect from therapy directed to syphilis is produced upon the symptoms and signs due to hepatic disease, the conclusion seems warranted that the coexistence of the two is more than a coincidence. Such was the conclusion in Case II, and such seemed clearly to be the case in the following instance.

Case IV.—In June, 1913, a man, aged fifty-three years, sought advice for "stomach trouble." He had never had any previous illness of consequence, except he recalled a venereal sore when he was eighteen, which was treated briefly and "cured." Since then he had remained perfectly well until the present trouble began. He had been ailing about eighteen months, complaining at the outset for months of vertigo like seasickness, so that for days at a time he would have to remain in bed. Recently this symptom had been less troublesome; but he complained particularly now of soreness, and tenderness over the pit of the stomach; and if he lay on the left side, he felt so much pain he had to turn back to the right. Appetite was good; he felt hungry all the time; his food did not distress; there was no nausea nor vomiting. He had lost about thirty-five pounds in weight, and had grown very weak; also, he had noted that in the last few months he had grown pale, sallow, and icteric. This patient had a greatly enlarged liver, palpable

across the upper abdomen, with a total area on percussion of 16 cm.; the lower edge was hard but rounded, and the surface smooth and regular, but quite tender. There was no ascites, and no other organic abnormality was found. The blood showed a triple X Wassermann reaction. After treatment by mercurial inunctions and potassium iodide internally (the patient declined salvarsan), this patient in three months gained twenty-two pounds, his liver dulness receded until it measured but 10 cm., and his symptoms all disappeared.

Here was a case of undoubtedly hepatic syphilis, not yet having reached the stage of ascites, marvellously improved by specific therapy. Its recognition by means of the Wassermann reaction clearly indicated the plan of treatment, and the treatment proved by its efficacy that the hepatic cirrhosis and the luetic infection were sequence and not coincidence.

But the recognition of cirrhosis of the liver does not always lead to a test for syphilis as a possible cause, and so valuable time may be lost and a true understanding of the facts comes too late. The following case is one that might possibly have been saved had it been estimated earlier at its real value.

Case V.—In August, 1913, a man, aged fifty-four years, was brought to Lane Hospital delirious and unconscious. Through his friends it was learned that he had always been well until a year before, when he vomited a quantity of blood; and since then he had gradually "run down," growing steadily thinner and weaker and less and less able to attend to his work. Two weeks before coming to the hospital he grew so weak he had to go to bed, became drowsy and delirious and remained so from that time on. On examination he was found to be greatly emaciated and slightly icteric; there was a moderate ascites, with atrophied liver and enlarged spleen; no signs of disease in the heart, but dulness and rales at each pulmonary base; the urine showed a heavy cloud of albumin, with many hyaline and granular casts. He was found to have a daily persistent rise of temperature, from 100° each morning to 103° each afternoon; his blood showed 21,600 leukocytes to the cm., with 88 per cent. polymorphonuclears. After coming to the hospital he lived but three days. The diagnosis made was cirrhosis of the liver, with ascites and with terminal toxemia. The report on the Wassermann reaction was not received prior to death. Autopsy revealed a liver shrunken to half its normal size, nodular and irregular, with many fibrous strands running through it, and a spleen about twice the normal size, studded with small abscesses, subsequently proved to be broken-down gummata. Both lungs showed a terminal pneumonia, which was the direct cause of death, and which accounted for the toxemia, the fever, and the leukocytosis.

If this man's condition had been recognized a year earlier, when he had his hematemesis, there would have been some prospect of

saving his life. Even then, however, the diagnosis would probably have been simply cirrhosis of the liver and the real etiology would have escaped notice, for there was nothing in the man's past history, his manner of life, or his previous ailments to cause any suspicion whatever of lues; if one depended only upon old routine methods of investigation, no other conclusion than cirrhosis could have been reached.

The final case observed illustrates how the error of overdiagnosis may be made and a conclusion reached that is even more serious than the facts warrant, rather than less so.

CASE VI.—A woman, aged forty-three years, was brought from the country in September, 1913, for examination, because her husband had been told she had cancer and her case was hopeless. She had been married for twenty-six years, but never had a pregnancy. Though always of small frame and low energy, she had never had any serious disease. For eight years she had had chronic "stomach trouble," her food souring soon after it was eaten, with occasional vomiting of material very irritating to the throat, and her sleep habitually disturbed by gas in the stomach and distress. She never had weighed over one hundred and twelve pounds, but there had been no recent loss of weight of any consequence. The patient was small, poorly nourished, pale, and sallow. No abnormality was found in any organ except in the abdomen; but there was found a marked bulging over the right lower thorax and upper abdomen; dulness on percussion from slightly below the nipple level to the level of the navel, 21 cm. in all; the lower border of this mass was palpable as a sharp, hard edge; the surface smooth but very tender. The spleen apparently was not enlarged. The abdomen showed a small amount of free fluid present. The stomach was displaced downward but not dilated, with no evidence of food retention, and a moderate subacidity; total acidity, 30 per cent.; free HCl, 12 per cent.; combined HCl, 10 per cent. The Wassermann reaction was a triple X positive one. On these findings it seemed reasonable to assume that her true condition was hepatic syphilis and not cancer. Too short a time has since elapsed to put the matter to the therapeutic test.

CONCLUSIONS.—The lessons to be learned from the foregoing histories are the following:

1. In any case that appears to be cirrhosis of the liver, judging from clinical history and physical signs, the blood should always be examined for syphilis. If the Wassermann reaction is positive, vigorous specific treatment will often produce marvelous improvement not to be expected in any other way; but even when the reaction is positive, the liver disease may not be luetic, and so specific therapy may prove of no avail; yet at the same time the therapeutic test will have given valuable information and have done no harm.

2. There is no certain way to tell which case of hepatic cirrhosis is luetic and which is not, except by the blood test, for previous history of infection, or of other earlier manifestations of syphilis, as well as stigmata produced elsewhere in the body by the disease, may all be lacking absolutely; while there may be nothing about the condition of the liver on physical examination or the symptoms it produces, to determine the etiology or to distinguish ordinary portal cirrhosis from luetic.

3. Syphilitic cirrhosis of the liver is a common form of hepatic disease, and must never be forgotten in the differential diagnosis of any case where symptoms and signs point to the liver as the organ involved.

SYPHILIS OF THE VERTEBRAL COLUMN: ITS SYMPTOMATOLOGY AND NEURAL COMPLICATIONS.[1]

By J. Ramsay Hunt, M.D.,

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Introductory Remarks. Syphilis is recognized as a fairly frequent occurrence in certain portions of the skeleton, more especially of the tibia, clavicle, and skull. All authorities agree that involvement of the spinal column is very rare, and some writers even regard its occurrence in the dorsal and lumbar regions as somewhat doubtful. This spirit of skepticism is probably due to the fact that many of the cases formerly recorded as syphilitic were really tubercular in nature, and many such errors of interpretation are to be found in the earlier literature. In the past few years, interest in this question has been revived, and the condition while unquestionably more frequent than is generally held, is nevertheless a comparatively rare affection.

At the present time, there are about one hundred well-authenticated cases recorded in literature, from which may be obtained a fair idea of its frequency, localization, and symptomatology.

The first statistics on this subject were published by Neumann in 1904, giving an analysis of 55 cases. The vertebral localization was as follows:

Cervical region	36 cases
Dorsal region	9 "
Lumbar region	8 "
Sacral region	2 "

[1] Presented at the meeting of the American Neurological Association, June, 1912.

Of the cervical group, in all but 8 cases, the disease was localized in the four upper vertebræ, a majority of these involving the axis and atlas.

Petren, in 1909, again analyzed the existing cases, and in his series the same frequency of involvement in the cervical region is shown:

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In this series the number of vertebræ affected in a given case was also tabulated, which shows a decided tendency to limitation of the process within a circumscribed area.

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1 vertebra in	25 cases
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Cases of syphilitic disease of the spine have also been recorded by Fry and Sachs in this country, which with 4 personal observations and those of Oppenheim not included in the previous statistics, bring the total number of available cases up to 100.

The great frequency of the cervical localization has been noted by all writers on this subject. Gerhardt has suggested that this frequency may be due to the proximity of this region to the bones of the skull, and as a consequence the extension of the disease downward. Another potent factor has been the secondary involvement of the upper cervical vertebræ by direct extension from pharyngeal ulcerations and gummata. This is especially true of the older cases, in which sequestra and fragments of necrosed bone having this origin were not infrequently expelled through the mouth. Neumann regarded the extension from pharyngeal ulcerations as the chief cause of cervical involvement in the majority of cases.

That the dorsal region may also be the seat of the lesion is shown conclusively by one of Oppenheim's cases, with involvement of

the eleventh and twelfth dorsal vertebræ and spinal-cord complications, as well as a more recent observation by Preiser. In Case IV of my series there was syphilitic osteitis of the lower lumbar vertebræ and sacrum, confirmed by pathological examination.

The *x*-rays will probably play an important role in the future diagnosis of this disease. In one of Petren's cases the diagnosis was confirmed by this means, and Sachs has emphasized the importance of this method.

In two of my cases with severe vertebral symptoms, no bone lesions could be demonstrated in the radiogram, and the bone involvement was evidently more in the nature of a periostitis (perispondylitis). In another, however, definite lesions, exostoses with thickening of bone tissue, were found.

The pathological lesions in the vertebral cases are the same as are found elsewhere when the skeleton is involved, and consist of exostoses, gummatous periostitis, and osteomyelitis, with occasional necrosis and sequestration of bone. The tendency to pus formation is slight, and "cold abscesses" as found in tubercular caries apparently do not occur.

It is evidently rare for the spine to be affected in the second stage of syphilis, the greater number originating in the tertiary period. Petren has described a case occurring in an infant with secondary lesions. Neumann maintains that hereditary lues may be localized in the spine, and records four cases between the ages of four and eleven years.

The *symptomatology* of syphilitic spondylitis does not differ essentially from that accompanying other affections of the spine, and consist essentially of pain, tenderness, rigidity, and deformity. In some cases, more especially in the cervical region, firm, nodular swellings may be palpated (exostoses). Tenderness appears to be more marked than is usual in tubercular spondylitis, and the nocturnal osteocopic pains are particularly persistent and distressing.

In cervical involvement it has been remarked by Petren and also by Ziesché that rotation of the head is more restricted than flexion; the reverse was true in one of my cases.

One of the most interesting questions of symptomatology is the frequency and nature of neural complications resulting from invasion or compression of the spinal cord and nerve roots. Of the 100 cases which I analyzed, neural symptoms were present in 26, distributed as follows:

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technical methods of the present day, which serve to detect the milder grades of pressure both of the cord and nerve roots.

The neurological examinations in this series of cases are by no means complete, so that a detailed analysis is impossible, but a general idea may be obtained of the nature and extent of the injuries sustained by the neural structures.

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In 9 cases the limitation of symptoms to paralysis and paresthesia of one upper or lower extremity indicated a radicular origin. Such an involvement of the roots or plexus producing monoplegia alone must be a rare occurrence in Pott's disease, and when it is present should arouse the suspicion of syphilis.

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Similar cases are also met with in the lumbar region, and may be unilateral or bilateral in distribution, due to involvement of the nerve roots or adjacent plexus.

It is interesting to note in passing that parasyphilis may also be complicated with syphilitic spondylitis (Hallopeau and Sachs).

Of special complications which may occur the most noteworthy is ulceration of the pharynx which was observed in 16 cases of the cervical localization (Neumann), and which gave rise in 9 cases to extrusion of fragments of necrosed and carious bone. Sudden death has occurred from erosion of the vertebral artery (Mackenzie), and once from ulceration and rupture of the internal carotid (Landrieux).

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these came on suddenly in the upper cervical region, simulating rheumatic myositis; x-ray examination was negative; girdle pains around the base of the neck and lancinating pains in the distribution of the occipital nerves were the only nerve complications; gradual subsidence of pain under antisyphilitic treatment; rigidity persisted for some months, but gradually disappeared with complete restoration of functions.

History. The patient, a man, aged forty-three years, an expert accountant by occupation, was referred to me on April 7, 1910, by Dr. Frank W. Murray, for severe headache which had persisted for over a year. He had pneumonia at the age of seventeen years and typhoid fever at thirty-two years, following which there was slight deafness with occasional tinnitus in the right ear. He is moderate in the use of alcohol, and denied emphatically any venereal disease. One brother died of tuberculosis, but this is the only occurrence in the family history worthy of special mention.

In January, 1909, he had a throat trouble, accompanied by huskiness of voice, which was diagnosed as a possible tubercular lesion of the larynx. His family physician, however, suspected syphilis, and under moderate doses of potassium iodide all symptoms disappeared. Coincident with the laryngitis there developed frontal and temporal headaches, which were always most severe at night, and these have continued with occasional remissions up to the present time. Because of the nocturnal character of the pain it was his custom to sleep during the day, as sleep at night was impossible, owing to the intense pain. He had noticed that while taking the potassium iodide the headaches seemed less intense, but this treatment had been intermittent, and the drug had never been taken continuously or in large doses. After a time three small round prominences appeared on the left frontal bone (exostoses). He stated that in the autumn of 1908 he had had pain and swelling of the left knee-joint, which gradually subsided. At the present time the knee-joint is swollen, and there is a slight effusion in the joint; there is also a very tender point over the patella. He has never had any vomiting or vertigo with the headaches, which were distinctly nocturnal and osteoscopic in character. There were no other cerebral or nervous symptoms present.

Status Præsens. April 7, 1910. The pupils are equal and react promptly. No tremors. Skin and deep reflexes are normal, as as are the cranial nerves. The deafness on the right side is of the middle-ear type. Optic disks are normal. Urine is normal. Examination of the viscera proved negative. The Noguchi test of the blood gave a positive reaction. Corresponding to the site of one of the small projections of bone noted by the patient in the left frontal region a small depression in the skull can now be palpated. Clinically the case is clearly one of bone syphilis involving the cranium and the articulation of the left knee-joint. He was

placed upon ascending doses of iodides, with hypodermic injections of the salicylate of mercury.

May 12. Under mixed treatment the headaches promptly ceased; the swelling of the knee-joint subsided, but has not entirely disappeared, and he still has occasional pains in the joint.

June 30. There is still slight swelling and some tenderness of the knee-joint. No cranial pain.

August 1. Owing to intestinal symptoms, the iodides and mercury were omitted.

September 1. Pains in the knee and skull have entirely disappeared. Wassermann reaction was strongly positive. He was told that he unquestionably had syphilis, and should undergo a prolonged and systematic course of treatment. He did not take this advice seriously, and did not return until January 21, 1911, when he appeared with a puffy edema over the right eye, which had developed suddenly and under which the bone was tender to pressure. There was little or no spontaneous pain. He had had no antisyphilitic treatment since the previous July.

The swelling subsided rapidly under antisyphilitic treatment, after which he did not return until October 12, 1911. At this time he complained of no symptoms, and the Wassermann reaction was negative.

October 16, 1911. He returned with a painful and stiff neck of three days' duration, which had appeared suddenly after sitting in the open air for two hours in a strong wind, watching a base-ball game. He had with it a sore throat and a general feeling of having taken cold. In view of the negative Wassermann reaction on October 12, and a very clear history of exposure to cold with sore throat, he was placed upon antirheumatic treatment, although with the previous history the possibility of lues was held in reserve. As little or no improvement followed the usual local and general treatment for rheumatic myositis, he was again placed upon antisyphilitic treatment.

November 1. At this time the movements of the neck were restricted in all directions, and caused considerable pain (see Fig. 1). There was distinct tenderness over the second and third cervical vertebræ, also on deep pressure on both sides of the spinous processes. Opening the mouth caused sudden pains in the occiput. There has also developed a tender and painful spot over the right parietal bone. Sharp, shooting pains are felt in the course of both occipital nerves. He also complained of a tight band-like drawing sensation around the sides and base of the neck (neck girdle). Swallowing caused painful sensations in the lower occipital region. Pain is much worse at night, coming on about five o'clock in the afternoon. In the morning he is fairly comfortable.

November 11. Movements of the neck are a little less restricted. The second cervical segment is still tender on pressure. Girdle

sensation is also present about the root of the neck, and jarring of the spine causes shooting pains in the right occiput and auricular region. The painful spot over the parietal bone is still tender.

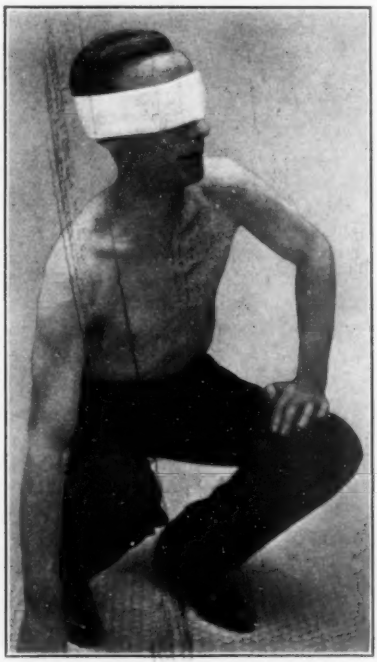

FIG. 1.—Syphilitic spondylitis of cervical region. Case I. Patient picking up an object on the floor, showing marked rigidity of the neck and fixation of the head.

x-ray examination by Dr. L. G. Cole, who reports as follows: "Structure and contour of the bones of the head and neck show distinctly. Bodies of vertebra and intervertebral foramina are quite distinct. In the lateral direction the bodies of the third, fourth, and fifth vertebræ are normal in size, shape, and alignment. There is an unusual space between the anterior ring of the first vertebra and the body of the second vertebra, and the relation of the odontoid process to the anterior ring of the first cervical vertebra is altered. In addition there is a spur on the upper surface of the ring which forms the partial foramen through which the first nerve emerges from the spine. This spur is to be regarded as an anomaly. Otherwise the examination is negative. I am unable to detect any change in the structure of these bones which would indicate that it is of syphilitic or tubercular origin.

November 17. He is generally free from pain in the early part of the day, but it returns about four or five o'clock in the afternoon. It is burning and throbbing in character. The neck is much more flexible, especially backward and forward. It is, however, held stiffly. Tenderness of the second and third cervical vertebræ has practically disappeared. Jarring of the spine causes shooting pains over the mastoid on both sides.

January 19, 1912. A second *x*-ray examination was made by Dr. E. W. Caldwell, who reports as follows: "I made a number of *x*-ray plates showing the lower six cervical vertebræ very well. I do not find any indication of the cause of his symptoms, in this part of the column, but I suspect that the trouble is in the articulation between the axis and the atlas, the shadow of which is obscured by the shadow of the skull. The limited rotation in this joint makes it practically impossible to secure an *x*-ray shadow of it which is not obscured by superimposed shadows of the other bones."

March 5. Neck is still stiff, but has steadily improved. The lateral movement is more restricted toward the right. There is still some deep-seated tenderness over the second and third cervical spines.

Remarks. Under the continuation of antiluetic treatment, pain and tenderness entirely disappeared. For some months the movements of the neck were restricted, especially flexion and extension, but after a course of osteopathic treatment (taken on his own initiative) this rigidity entirely disappeared. He is still unwilling to believe that the disease is syphilis, and now that he is well he is averse to taking further precaution or treatment.

The onset of vertebral symptoms in this case had been preceded during the previous three years by a train of symptoms clearly indicating syphilitic involvement of the cranial bones, the knee-joint, and the larynx. All of these various manifestations subsided under antiluetic measures. While a specific infection was denied, the Wassermann was positive. From these clinical facts there can be no question as to the syphilitic nature of the subsequent symptoms in the cervical region. The process was apparently localized in the upper three cervical vertebræ, judging from the local tenderness, which was quite marked, and the root pains and girdle sensations of the neck which corresponded to these levels. There were no symptoms pointing to involvement of the spinal cord.

One of the interesting features of the case was the sudden onset following exposure to cold, so that the clinical picture closely resembled rheumatic torticollis. The subsequent course served to demonstrat its true syphilitic nature.

Two examinations were made by the *x*-rays, both of which failed to reveal any lesions of the bone tissue.

I have, therefore, regarded the process as being in the nature of a syphilitic periostitis or perispondylitis, with compression of the adjacent nerve roots. The pain on pressure and jarring of the spine, the local tenderness and rigidity, were so characteristic of vertebral disease as to rule out a syphilitic pachymeningitis with root involvement.

CASE II.—*Syphilitic periostitis or perispondylitis of the cervical region, with pain and rigidity of the neck, motor and sensory disturbances of the right upper extremity, distinct tenderness and thickening in the lateral region of the cervical column.*

History. Patient is an Italian, aged twenty-seven years; a barber by occupation. He was admitted to the New York Hospital, August 14, 1907, where I saw him on several occasions in consultation with Dr. Conner, the attending physician.

Previous History. In 1898 he contracted a venereal ulcer, for which he received only local treatment. No secondaries were noted by the patient. He remained in good general health until March, 1902, when headaches appeared. At first in the left frontal region, later becoming general. They were quite severe, with marked nocturnal exacerbations. He was admitted to the New York Hospital, March 22, 1902. Physical examination is negative, except for a double optic neuritis. The diagnosis of cerebral syphilis was made, and all symptoms cleared up rapidly after a course of mercury and iodides.

On December 1, 1903, he was readmitted to the New York Hospital with headaches of one month's duration, situated chiefly on the right side of the head in the temporal region. The headaches were quite severe. There were distinct nocturnal exacerbations, with tenderness on pressure over the right parietal bone, but no bony nodules could be felt. He also had some pain in the anterior aspect of the left thigh and of the left leg. There was no vertigo, vomiting, or diplopia. The optic disks were normal. The general physical examination was negative, save for some secondary anemia (hemoglobin, 60 per cent.). After a short course of antisyphilitic treatment the symptoms completely disappeared and the patient was discharged. A clinical diagnosis of cerebral syphilis was made.

Present Illness. Patient was re-admitted to the New York Hospital August 14, 1907, with the following history: For the past seven months he has had pains in the back and sides of the neck and in the left shoulder, gradually becoming more severe. For three months he had been unable to work. The left elbow is slightly swollen and tender and is the seat of occasional spontaneous pain. He also has headaches, and because of the nocturnal increase of the pain, sleep has been almost impossible for many weeks. For the past five days, he has had severe pains in the region of the right shoulder, and has developed a weakness, with

paresthesia of the right upper extremity. The neck is also stiff, and the movements are painful. There is no vertigo, vomiting, nor diplopia; no vesical trouble.

Physical Examination. The gait and station are normal, except for an evident stiffness of the neck and fixation of the head. The movements of the neck are restricted in all directions, and cause considerable pain. The cervical spine is quite tender to pressure on both sides, especially on the right. The spinus processes, however, are not tender on percussion. Jarring of the spine causes pain, which is referred to the cervical region. The movements of the dorsal and lumbar spine are free and painless. The pupils are equal and react to light and accommodation. There are no cranial nerve palsies or nystagmus, and the optic disks are normal. There is considerable weakness of the right upper extremity, and especially in the movements of abduction and elevation of the arm. Sensations to touch, pain, and temperature are diminished over the whole of the right upper extremity. There is marked tenderness along the lateral portion of the cervical spine where the nerves emerge from the intervertebral foramen, but especially on the right side. Palpation also shows some general thickening and enlargement in this region of the spine. Both shoulder-joints are freely movable and painless. The left elbow-joint is freely movable, but is slightly swollen and tender. There are no tender spots on the skull. All tendon and skin reflexes are present and normal. There is plantar flexion of the toes on both sides (no Babinski). Examination of the heart, lung, and urine are negative. The blood shows slight secondary anemia (hemoglobin, 84 per cent.). The *x*-ray examination of the cervical spine was entirely negative. The temperature curve showed a slight elevation for the first few days, after which it remained normal. Wassermann reaction was positive.

Subsequent Course. The patient was placed upon antisyphilitic treatment, hypodermics of salicylate of mercury, and ascending doses of potassium iodide. There was a rapid subsidence of all symptoms.

August 27. The pains had diminished, and the movements and sensation of the right upper extremity were normal. Some stiffness of the cervical spine, with pain and tenderness, still persisted.

September 14. Pain had practically disappeared. Can now move the head in all directions, but the movements are still somewhat restricted, and there is still present some lateral thickening in the cervical region, which is tender to pressure.

Patient was referred to the out-patient department for further treatment, and eventually made a complete recovery.

Remarks. The vertebral symptoms in this case had been preceded by two previous attacks, diagnosed as cerebral lues, both of which cleared up completely under antisyphilitic treatment. The verte-

bral symptoms came on gradually, and were of seven months' duration, and were limited to the cervical region. There was in addition to rigidity and pain on jarring in the cervical region, marked tenderness along the lateral aspect of the vertebræ where the nerve roots emerge. This was especially localized upon the right side, where a distinct thickening and enlargement was palpable. The neural symptoms made their appearance about six months after the onset of the vertebral disease, and were evidently of root or plexus origin. They consisted of weakness, with objective sensory disturbances in the right upper extremity. There were no evidences of spinal-cord involvement. All symptoms subsided under specific treatment.

CASE III.—*Syphilitic spondylitis of the upper cervical region; sudden onset, with pain and rigidity in August,* 1907; *improvement under specific treatment; frequent recurrences of pain and stiffness from lack of continuous treatment; in December,* 1910, *development of acute symptoms with vomiting, vertigo, and headache, followed by numbness and weakness on the right side, and an atrophic paralysis of the left side of the tongue (hemiplegia alternans); improvement under antisyphilitic treatment; in November,* 1911, *there was still rigidity, with thickening and enlargement in the cervical region, and the residual symptoms of hemiplegia alternans.*

History. The patient, a negro, aged thirty-seven years; occupation, bellboy; was admitted to the Vanderbilt Clinic, department of nervous diseases, on November 18, 1911. He is married and has one child, aged six years, living and well. His wife has never miscarried.

Six years ago (1905) he contracted syphilis; no general treatment. In August, 1907, he was seized suddenly with pain in the occipital region and in the nape and sides of the neck, which was followed by rigidity and stiffness of all the movements of the head. At the medical clinic where he applied for treatment the case was first regarded as rheumatic myositis, but because of the previous specific infection, he was later treated with iodide of potassium and mercury. The pain rapidly subsided and the rigidity was greatly diminished. Following this improvement, he failed to return for further treatment, although some stiffness of the neck still persisted, and from time to time he had pain in the cervical region. When the pain was severe, he would return for medicine, and after taking the iodides for a short time, the pain ceasing, he would abandon the treatment. When the pain was severe, the neck seemed to be swollen and slightly enlarged in the painful areas.

In November, 1909, he suddenly developed cerebral symptoms; frequent attacks of vomiting, with headache and vertigo. The vomiting was severe and of the cerebral type, and had persisted for two weeks before he was admitted to Roosevelt Hospital, on November 24, 1909. These general cerebral symptoms were soon

followed by weakness and paresthesia of the right arm and leg and some thickness of speech, due to a paralysis and atrophy of the

FIG. 2.—Case III. Old syphilitic spondylitis of the cervical region, showing rigidity of neck and slight torticollis position of the head.

FIG. 3.—Case III. Syphilitic spondylitis of cervical region, posterior view.

left side of the tongue (hemiplegia alternans). The heart and lungs and urine were reported negative in the hospital history.

The Wassermann reaction was negative on December 17, 1909. There was rigidity, with moderate thickening and tenderness, along the lateral aspect of the cervical region of the spine. The general cerebral symptoms cleared up promptly under antiluetic treatment. The patient was discharged with the symptoms of hemiplegia alternans persisting. There was still some stiffness of the neck and an occasional pain, especially at night.

November 18, 1911. Patient returned to the Vanderbilt Clinic, complaining of pain and stiffness in the cervical region, and was referred to the Neurological Clinic, where he came under my observation.

Physical Examination. The head is in a slightly torticollis position, the chin directed toward the left (see Figs. 2 and 3). All movements—rotation, flexion, and extension—are restricted. Jarring of the spine causes pain in the upper cervical region (first, second, and third cervical). There is some thickening in the region of the lateral processes on both sides of the neck, especially on the right. There is a slight compensatory lateral curvature of the spine. Pupils are equal and react normally. Ocular excursions are normal except for a slight lateral nystagmus. Vision and the sense of smell are normal, as are the fifth and seventh nerves. There is diminished hearing on the right side (central deafness). The soft palate is equally enervated on the two sides. The tongue deviates sharply toward the left. There is a very pronounced atrophy, with deep furrows and marked fibrillation of the left side of the tongue. There is also some atrophy, with fibrillary twitchings on the right side as well, but to a lesser degree. There is no difficulty in deglutition, and the voice is normal. No laryngoscopic examination. The sternocleidomastoid and trapezius are normal on the two sides. The right arm and leg show some weakness, more especially the leg. The tendon reflexes of the right lower extremity are exaggerated, and there is ankle-clonus. No patellar clonus. The plantar reflex on the right side is diminished, and is of the flexor type. It is normal on left. The abdominal and cremasteric reflexes are diminished on the right side. The superficial sensibility is lost over the right lower extremity and over the lower half of the right side of the trunk; above this the sensibility is simply diminished. The sensibility of the face is normal. The deep sensibility of the upper and lower extremities is normal.

The man was placed upon anti-syphilitic treatment and the pain and stiffness in the neck rapidly improved. As was always the case in this particular patient, as soon as the pain ceased he lost interest in the treatment and ceased to continue it. There is, however, no question as to the rapid response at all times to anti-syphilitic treatment, especially the iodides.

An *x*-ray examination at the Roosevelt Hospital showed thicken-

ing and enlargement of the bodies of the third, fourth, and fifth cervical vertebræ, as well as of certain of the lateral processes, especially on the right side. There were no evidences of destruction or cavity formation of the vertebræ or intervertebral disks.

REMARKS. The syphilitic spondylitis in this case had run a very gradual course, extending over a period of four years. The chronicity of the symptoms and the permanency of the rigidity may be referred to the intermittent and incomplete manner in which the antisyphilitic treatment was carried out. This never failed, however, to produce subsidence of pain and diminution of rigidity.

An interesting and unusual feature is the occurrence of hemiplegia alternans, a unilateral atrophic paralysis of the tongue with contralateral hemiplegia, due to a lesion in the lower portion of the medulla oblongata on the left side. It is possible that this lesion of the medulla may have been caused by syphilitic disease of the vertebral artery as it coursed through the transverse process. Cerebral lues independent of the vertebral disease cannot, however, be excluded.

CASE IV.—*Syphilitic osteitis of the lower lumbar vertebra and sacrum, with gummatous infiltrations of the cauda equina, followed by paralysis and sensory disturbances, in the distribution of both sciatic nerves, and accompanied by marked rigidity, deformity, and tenderness of the lumbosacral spine; autopsy revealed syphilitic osteitis of the lower lumbar vertebra and sacrum, with multiple gummata of the cauda equina.*

History. Patient, a man, aged fifty-three years, was admitted to the Montefiore Home for Chronic Invalids, January 5, 1896. He denies all venereal disease, and enjoyed excellent health up to one year ago, when he developed pains in the distribution of the right sciatic nerve, which were especially severe at night. There was some tingling and numbness on the outer side of the right leg. A little later similar pains and paresthesia developed in the same distribution on the left side. He also had severe pain in the lower portion of the back over the sacrolumbar region, especially in the sitting posture, so that he was obliged to use a cushion to protect this region from pressure. Pain was particularly severe in the sitting or recumbent posture, and he would experience a little relief in standing and in walking. The pain became gradually more severe, and he was obliged to resort to narcotics and analgesics for relief.

On October 7, 1895, he was admitted to Mt. Sinai Hospital, and while there developed extensive paralyses of the lower extremities, with incontinence of urine and feces.

On his admission to the Montefiore Home, he complained of shooting pains in both lower extremities and severe pain in the lower portion of the spine, especially in the sitting and recumbent posture; incontinence of urine and feces and impotency.

Status Præsens (Dr. Joseph Fraenkel). Patient is unable to walk because of weakness in the lower extremities. On attempting to stand he complains of pain in the lower portion of the spine, and sudden pains in the feet and legs. There is a constant dribbling of urine. Pupils are small and equal; reaction to light slight; reactions on accommodation are present. Ocular excursions are normal. Motility, coördination, muscle volume, and sensibility of the upper extremities are normal. There is a well-marked kyphoscoliosis at the junction of the dorsolumbar region, the scoliosis being the more marked deformity. The spine is tender on pressure, beginning at the first dorsal vertebra and extending to the coccyx. This sensitiveness is especially marked over the eleventh and twelfth dorsal and the first lumbar vertebra and over the lower portion of the sacrum. It is acute on percussion. Over the lower portion of the sacrum there is a slight tumefaction. The movements of the column show great rigidity, and are accompanied by considerable pain. There is no visible atrophy nor fibrillation of the muscles of the back. There is some weakness of the abdominal muscles in their lower portion. Both lower extremities are paretic, more especially the left. The calves of both legs are markedly atrophic. The knee-jerk is lively on the right side, with patellar clonus; absent on the left. Both ankle-jerks are absent. The abdominal, cremaster, and plantar reflexes are absent on both sides.

Sensation. There is tactile and thermal anesthesia in the distribution of both sciatic nerves. Sensibility to pain is diminished in the same area. There is also anesthesia of the left buttock, left side of the scrotum, and penis and perianal region. The deep sensibility of the toes is disturbed. Heart and lungs are normal.

Death occurred February 28, 1896. Postmortem examination showed extensive syphilitic osteitis of the lower lumbar vertebra and the upper portion of the sacrum. There was a good-sized erosion of the first sacral segment. The strands of the cauda equina were matted together by extensive syphilitic infiltrations, and contained four gummata the size of hazelnuts. The histological examination of sacral segment and cauda equina present the typical lesions of syphilis.

Remarks. This case is interesting because of its unusual localization, syphilis of the lumbar region being the rarest of all types. Cases of syphilitic caries of the sacrum have been described by Yvaren and by Westphal. In Westphal's case it was associated with typical sacral anesthesia.

Concluding Remarks. Syphilitic spondylitis and perispondylitis while rare are nevertheless sufficiently frequent to be given careful consideration in every case of acute or chronic vertebral disease. The onset may be sudden, simulating an acute rheumatic affection, or it may develop gradually and run an exceedingly chronic and protracted course.

Localization in the cervical region, especially, should awaken the

suspicion of lues, as more than half of the recorded cases are of this region. It may, however, occur in any portion of the spinal column.

Of 100 cases available for analysis, I found that 25 per cent. were associated with some complication referable to the nervous system. These were either of the nerve roots and plexus or of the spinal cord itself.

Generally speaking, in this group of cases with neural complications, the symptoms indicated a lesion of the spinal cord in two-thirds; in the remaining third, the neural symptoms were limited to an involvement of the nerve roots or plexus.

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SYPHILIS OF THE ESOPHAGUS.

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It is a well-established clinical fact that in a given individual, certain of the systems seem more predisposed in their susceptibility to the Spirocheta pallida than do others. The peculiar predisposition for the exclusive localization in the nervous system, for example, occurs in those cases in which the mucocutaneous system is relatively uninvolved, and, conversely, where the mucocutaneous system is early involved with severe manifestations it is exceptional to find late nervous sequelæ. To what extent this susceptibility is due to the virulence or strain of the organism, on the one hand, or to the individual lowered resistance of the affected system, on the other, is as yet undetermined.

The high susceptibility of the mouth and pharynx in early syphilis and the not infrequent occurrence of syphilitic manifestations in the rectum late in the disease make the apparent immunity of the rest of the digestive system a rather striking feature. Leaving out the mouth and rectum the digestive tube seems to enjoy an immunity to the action of the syphilitic organism which is without parallel in any other system. Syphilis of the esophagus, of the stomach, and small intestine is of exceedingly rare occurrence. Indeed its occurrence was denied in many of the earlier works on pathology, surgery, and medicine.

The first mention of syphilis of the esophagus is found in the writings of Severinus[1] in the middle of the eighteenth century. Gastou,[2] who wrote the chapter on syphilis of the gastro-intestinal system in Fournier's monumental work, has been able to collect 40 cases of esophageal syphilis. In 13 of these cases the diagnosis could be verified at autopsy; 6 cases improved under the influence of antisyphilitic treatment and did not come to autopsy; in 11 cases there was dysphagia, with the signs of stricture, and 10 cases of the 40 Gastou holds open to doubt as to the correctness of the diagnosis.

Dysphagia, leading to marasmus and death, in the course of syphilis is mentioned by Jean Astruc[3] (1736) and also by Carmichael[4] (1815). Ruysch[5] (1717) and Haller[6] (1768) report cases in which apparently syphilitic stenosis of the esophagus was cured

[1] Cited by Lublinski, 1580–1636 (Berl. klin. Woch., 1883, pp. 499 and 515).
[2] Traite de la Syphilis, A Fournier, 1906, ii, 465.
[3] De Morbis venereis libri sex, Paris, 1736.
[4] An Essay on Venereal Diseases, Dublin, 1815, p. 270.
[5] Adv. anatomico medica chiurgica, Amsterdam, 1717–1723. (Cited by Lublinski.)
[6] Opuscula pathologica, etc., Laus, 1768. (Cited by Lublinski.)

by mercurial treatment. The anatomy of esophageal syphilis was first described by Lieutaud.[7] Notwithstanding these early reports of esophageal syphilis, many of the earlier texts on pathology and surgery failed to give a place to syphilis of the esophagus. In Bardeleben's[8] text, however, also in Strümpell's,[9] ulcerations of the esophagus due to syphilis are described. Koenig,[10] writing in Billroth's *System*, also gives mention to esophageal syphilis. The subject receives considerable mention in *Virchow's Archiv* by Virchow[11] himself. Herein are included the autopsy report and the full anatomical description of esophageal stenosis in syphilis and of esophageal ulcerating gumma.

In 1863 Wilks[12] showed a specimen from the museum of Guy's Hospital which showed sclerosis of the upper portion of the esophagus following syphilitic ulceration. The same observation is recorded in 1875 by Klob.[13] The first, however, to call attention to esophageal syphilis in an excellent monograph was James West[14] (1860). This author collected from his vast experience three cases of syphilis of the esophagus, in two of which he was able to corroborate his clinical findings at autopsy. The other case improved on treatment and remained well. West cites also in his paper cases by Langston-Parker[15] and Clapton,[16] which by analysis could be nothing but cases of syphilitic esophagitis.

Follin,[17] in 1861, records a case of dysphagia of undoubted syphilitic nature. Robert,[18] in 1861, cited by Lubinski, in discussing dysphagia in syphilis, avers that the autopsy findings in such cases show at times lesions in the pharynx, in the larynx, and in the esophagus. Morrell MacKenzie,[19] in 1874, reports a case of esophageal stenosis at the level of the sixth dorsal vertebra in an old syphilitic which yielded in a short time to antisyphilitic medication. A most excellent treatise on the subject is published in 1883 by Lublinski,[20] who has cited literature at great length and added two observations of his own. Both these cases recovered completely, but there could be no doubt from the excellent description and history that these were examples of true syphilitic esophagitis.

[7] Historia anatomico medica sistens numerosissima cadavernum humanorum exstirpitia, Paris, 1767.
[8] Lehrbuch der Chirurgie und Operationslehre, 8th edition, iii, 543.
[9] Lehrbuch der speciellen Pathologie u. Therapie inneren Krankheiten, 1912, 18th edition, i, 518.
[10] Handbuch der allgemeine u. specielle Chirurgie, Pitha u. Billroth, 1880, iii, 17–18.
[11] Archiv f. pathologische Anatomie u. Physiologie, 1856, xv, 217–315.
[12] On the Syphilitic Affections of the Internal Organs, London, 1863, p. 41.
[13] Wien. med. Woch., 1875, xxv, 210.
[14] Dublin Quart. Jour. Med. Sci., 1860, xxx, 29; ibid., Lancet, 1872, ii, 291.
[15] Lancet, 1872, ii, 292.
[16] St. Thomas' Hosp. Rep., 1871, new series, ii, 177.
[17] Traite Elémentaire, Paris, 1861, i, 696.
[18] Nouveau Traite des maladies veneriennes, Paris, 1861.
[19] Lancet, 1874, i, 754.
[20] Berl. klin. Woch., 1883, pp. 499 and 515.

In 1887 a typical case is described by Potain.[21] According to Gastou,[22] gastrotomy is reported for syphilitic stenosis in 1870 by Maury. In 1884 Jullien[23] published a monograph on esophageal syphilis based on nineteen authentic cases which he had collected. In the American literature a single case, according to other authors, is reported by Godon in 1880. I have been unable, however, to verify this observation, as the reference is evidently misquoted as to the date.

Apparent paralysis of the muscularis of the esophagus due to syphilis is described by Saundby[24] in recent literature. In the case described by this author and in another cited by him and described by Mott[25] there was sudden paralysis of the esophagus, as shown by dysphagia, without any stenosis, occurring in syphilitic individuals. In both cases there was evidently central nervous syphilis antedating the esophageal symptoms, and both cases responded well to antisyphilitic treatment. Strictly speaking, these cases would hardly be classed as disease of the esophagus itself, but have rather to do with the involvement of its innervation, directly referable to syphilitic disease of the central nervous system.

Careful study of the cases described and the one observation of my own which is to follow, reveal no single etiological factor for the occurrence of the lesions in the esophagus. The lesions occurred somewhat more often in men than in women, although it is a striking fact that all of West's cases occurred in females. In no case did injury seem to play any role. Of striking significance, however, is the fact that in a large number of cases there were lesions in the mouth and pharynx, suggesting either the continuity of the infection, or speaking more directly for the localization of the process in the digestive system. It is also a striking fact that many of the earlier cases were evidently fulminating in type with rupia and extensive caries. Such are the cases described by Wilks, Carmichael, and West.

The pathology of syphilitic esophagitis depends upon the time at which the case may be studied. Secondary superficial erosions and ulcerations, such as occur in the mouth and pharynx are not described in the esophagus. Such cases do not come to autopsy frequently. The not infrequent dysphagia, however, that occurs in secondary syphilis could, I think, well be due to superficial erosive syphilides. The great bulk of our cases, however, are those of tertiary syphilis. Here it would seem that the process is usually a gummatous condition of the submucosa which undergoes one of

[21] Gazette Médicale de Paris, 1887, iv, 193; ibid., La Semaine Médicale, 7, 1887; vii, 261.

[22] Loc. cit.

[23] Loc. cit.

[24] British Med. Jour., January 31, 1914, No. 2770, p. 239.

[25] A System of Syphilis, Power and Murphy, iv, 92.

two changes. It may, under appropriate treatment, or even spontaneously, involute by fatty degeneration, such as is described by Lublinski and by West, the second case of Follin's, and in the case cited by West of Clapton's. In the event, however, of no treatment, or occasionally in spite of treatment, such gummatous changes are likely to undergo early ulceration. If these heal, there results a scar with a marked tendency to contraction and resulting stenosis. Finally, there may be, instead of localized scarring and contraction, a diffuse process encircling the entire tube for the greater part of its length and causing almost complete stenosis and impassibility for all solid food. This last condition is accurately described in the first of the Virchow cases and in the case described by Wilks.

To these cases we should like to append one which we have had the opportunity of observing at the University Hospital during the past year. The patient, a woman, aged forty years, was transferred to my department by my colleague, Dr. Canfield, of the Otolaryngological service. She was admitted to the hospital for throat trouble December 18, 1913. Her family history was of no importance save that the patient had had two miscarriages following two healthy pregnancies. Nine years previous to her admission she had ulcers on the left cornea, and finally the eye was removed. Eight or nine years ago the patient began to experience a little difficulty in swallowing. This did not become severe, however, until six years ago, when she would occasionally become choked on eating. There was also considerable pain at this time during the act of deglutition, and soreness of the mouth was noticed on taking of hot or sour food. At this time the glands of the neck were also considerably enlarged.

Status Præsens.—The patient is an extremely anemic, rather cachetic woman. The left eye is glass. The right pupil reacts to to light and in accommodation, but shows some interstitial keratitis. The skin of the body is entirely clean except for a few pigmented macules about the hips, knees, and back. The tongue is absolutely smooth and devoid of papillæ. The mouth is dry and there is extensive sclerosis of the entire buccal cavity. The entire mucous membrane of the mouth and tongue give the appearance almost of a kraurosis. There is no general adenopathy. The liver and spleen are not palpable. The urine and blood are normal. An *x*-ray plate of the patient's chest shows a periostitis about the middle of the left humerus. The occurrence of the esophageal lesion was accidentally discovered, as the patient did not complain of distinctly painful deglutition. On December 29 a small morsel of food became impacted in the esophagus and remained there one hour and twenty minutes in spite of efforts to dislodge it. At this time a small caliber stomach-tube was passed in order to relieve the patient of her dysphagia, and it was found that this could not

be passed into the esophagus at all on account of the very evident constriction just below the larynx. On December 30 an esophagoscopy was performed upon the patient by Dr. Canfield, and it was discovered that there was a marked sclerosis of the entire tube. Nothing but the smallest sized filiform bougie could be passed into the esophagus and down to the stomach. On January 17 the patient was given a bismuth paste and fluoroscoped. During the act of deglutition a definite stricture was noted just below the level of the lower portion of the larynx, and a second stricture just above the cardia. In both cases there was a distinct pouch found above the point of stricture and the bismuth could be seen passing very slowly through the constricted portions. An *x*-ray photograph was attempted and shows fairly well the uppermost of the two strictures. The patient was placed upon a combined salvarsan and mercurial therapy and her condition improved markedly. An attempt was also made to dilate the strictures with bougies of increasing size, and following each application deglutition was somewhat easier. At the present time the patient is receiving vigorous mercurialization and tri-weekly esophageal dilatation.

The symptoms of syphilitic esophagitis do not differ materially from the symptoms due to other forms of esophageal disease. Of first rank in importance is difficulty in deglutition. This, as a rule, is a gradual process. The patient notices at first slight difficulty in swallowing solid food. Then he can swallow solid food only in small morsels, and later solid food becomes impossible to swallow; it is regurgitated and liquid food only can pass into the stomach. In time this too becomes difficult, so that in rare cases there is complete stenosis. Pain is not a marked symptom, except during the act of swallowing. Where there is ulceration, pain may be present in repose as well as during deglutition. In old-standing cases where scarring and consequent narrowing of the tube occur the pain during attempted swallowing may be very severe.

Anemia, weakness, denutrition, and later cachexia are frequent late in the disease. These may find their cause either in coincident syphilis of other parts which is likely to approach a malignant type or, in cases in which an esophageal lesion is present without other manifestations of active syphilis, the above symptoms are readily explained on the ground of actual starvation.

The differential diagnosis is at times extremely difficult. In the absence of other manifestations of syphilis, carcinoma, compression of the esophagus by mediastinal tumors, and spastic stenosis are the conditions which are most readily confounded with the condition in question. The marked cachexia which may accompany the condition late, renders its differential diagnosis from carcinoma the more difficult. In general the carcinoma is apt to be more painful and appears more frequently in the lower part of the

esophagus than in the upper. Emesis and hematemesis are more common in carcinoma than in syphilis. The Wassermann reaction is of course a most valuable guide in the differential diagnosis. It must be remembered, however, that carcinoma could quite possibly find a starting place in an old gumma, so that a positive Wassermann, while presumptive evidence of the syphilitic nature of the process, would not of necessity rule out carcinoma. A valuable aid in the diagnosis as well as to the localization of the lesions lies in the *x*-ray and fluoroscopic examination. In the case described by myself the confirmation of the diagnosis was most satisfactorily established by this means. It was noted in the fluoroscope that bismuth taken a half-hour previously was

x-ray photograph showing the uppermost of the two strictures.

retained in two large pouches situated just above extensive areas of stricture. In the one case, as may be seen by the radiograph, the pouch is located just below the larynx. Just below this point the canal seems obliterated. The second pouch is noted about 6 cm. above the cardia, and from this point to the stomach the canal is again obliterated. This picture could obviously not be produced by carcinoma; that is, two extensive foci of disease separated by a relatively normal portion of the tube. The fluoroscope and radiograph would also serve obviously to distinguish such cases from those of simple spasm. The absence of shadows in the mediastinum and the absence of physical signs by percussion

readily differentiate the condition from mediastinal growths giving rise to esophageal compression.

The prognosis of the condition seems to depend entirely upon the time at which the condition is recognized. In those cases in which there is gummatous infiltration with a low grade of stenosis the prognosis under antisyphilitic is excellent. Where the gumma is ulcerated the prognosis is more grave, because it is sure to be followed by more or less constriction following the healing of such ulceration. In those cases in which there is extensive fibrosis of long standing the prognosis is exceedingly grave, and for the most part these patients die of marasmus.

The treatment of the condition must be a most energetic one. Up to the present time mercury and iodide have been of service in those cases in which a good prognosis could be looked for. In any event the esophagus should be carefully sounded following the antisyphilitic treatment, and the contraction, if there be one, should be gradually dilated much in the same way as in the treatment of urethral stricture. In my own case I may say that the patient improved markedly under the combined salvarsan and mercurial therapy, notwithstanding the fact that she belonged to the worst class of cases—namely, that in which there is complete fibrosis of the canal. The esophagus now admits a No. 11 bougie, the patient has taken on weight, eats solid food with greater ease, and is in a fair way toward partial recovery.

In conclusion I venture to express the opinion that syphilitic esophagitis, though a rare condition, is nevertheless not so infrequent as the rather scanty literature on the subject would seem to indicate. It is not improbable that many cases which die in cachexia supposedly with carcinoma of the esophagus are cases of death from marasmus as the result of syphilitic esophagitis. The same relation that Billroth showed between gumma and carcinoma of the tongue without doubt also exists in the esophagus. In these days of refined laboratory technique, however, mistakes in diagnosis are less apt to occur. It goes without saying that any case of esophageal stricture or esophageal tumor should not escape a most careful scrutiny, with a view to its possible syphilitic nature.

SCHISTOSOMIASIS JAPONICA: A CLINICAL AND PATHOLOGICAL STUDY OF TWO CASES.

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and

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To students of medicine in the temperate zones the swiftly advancing knowledge of the diseases peculiar to the tropics presented in such a work as Manson's *Tropical Diseases* has been more or less startling in its revelation of the widespread prevalence of diseases unknown in these parts, unique in etiology, and presenting entirely new problems in prophylaxis and treatment. So far as the etiology of these diseases has been revealed, it has been found to turn upon the activities of parasites, either bacteria or more highly developed organisms. So true is this that parasites come to occupy the mind of the student of tropical diseases, and we find Manson writing that "nearly all diseases, directly or indirectly, are caused by germs." The life-history of many of these parasites is most involved, and consequently the prevention and treatment of the resulting diseases present problems of great difficulty and interest. The constantly increasing movement of people from one part of the earth to the other carries with it the possibility that individuals suffering from some of the rarest of these so-called tropical diseases may be met with in this country, and a knowledge of these diseases may therefore become of importance to any physician.

It should also be said that the presence of infected individuals in this country renders it possible that parasites or germs heretofore limited to tropical distribution may be spread broadly here, and render endemic diseases heretofore unknown. Fortunately, however, the spread of these parasites seems to demand tropical conditions, or the presence of intermediary hosts peculiar to the tropics, so that thus far our knowledge of them has been limited to imported cases, such as the following:

Case I.—K. O., aged twenty-eight years; male; Japanese. Admitted to medical service of Presbyterian Hospital, November 21, 1910.

Family and personal history are negative.

Previous Illnesses. He has always been healthy except for some trouble with knees attributed by patient to beriberi, which lasted only one week. Five years ago he was in Bellevue Hospital seven weeks with a fever, the nature of which was not discovered. Since then he has been perfectly well.

Present Illness. He was perfectly well until the evening before admission, when about one hour after supper he began to feel queer and had a burning sensation in the stomach. At 9 P.M. he vomited. The vomitus consisted of the food eaten, mixed with some dark blood. He vomited again a little later, and still a third time; in each instance the vomitus contained dark blood. Aside from a queer feeling in the stomach and some burning in the upper abdomen, patient had no other symptoms. He slept, though not soundly, and this morning after taking some orange juice he vomited again one hour later, and still again about 10 A.M. Each time there was blood in the vomitus. No blood was ever noticed in the stools.

Physical Examination. Patient is markedly pale; mentally clear; well nourished. Breathing somewhat increased in rate. The skin, conjunctivæ, and mucous membranes are pale.

Heart: Normal size and position. Action is regular but quite rapid. Sounds are of fair quality; there is a faint systolic murmur at apex. Pulses are equal, regular, small, and soft. Rate 116.

Lungs: Normal.

Liver: Upper border; flatness is at seventh rib. Edge is not felt. Percussion is obscured by epigastric dulness and abdominal tympany.

Spleen: Enlarged to a point about two inches below the costal margin.

Abdomen: Rather full and hypertympanitic, with some abnormal dulness in epigastrium. Over the epigastrium there is some general tenderness. Otherwise the examination is entirely negative.

November 21. Urine: 1030; acid; very faint trace of albumin; a few leukocytes and epithelial cells.

November 21. Blood: Hemoglobin, 80 per cent.; white blood cells, 9100; polynuclears, 85 per cent.; lymphocytes, 12 per cent.; transitionals, 2.5 per cent.; basophiles, 0.5 per cent.

November 22. Hemoglobin, 68 per cent.

November 22. At 4.45 P.M. yesterday patient suddenly vomited a quantity of blood estimated at twelve ounces. An injection of morphine was immediately given. Again at 9.15 P.M. he vomited ten ounces of blood. An ice coil was applied to the abdomen and he slept quietly until 3.30 A.M, when he again vomited ten ounces. At 4 A.M., eight ounces, and again at 10.30 A.M., eight ounces of blood were vomited. After 11.30 A.M. he failed rapidly, and died at noon before an infusion could be given. An interesting feature was the fact that the spleen, quite large yesterday on admission, was much reduced in size this morning.

Autopsy, November 23 (by Dr. Cecil), twenty-five hours after death. The body is that of a young Jap measuring 150 cm. in length. Postmortem rigidity is present. Rigor mortis in dependent parts. Pupils are equal and moderately dilated.

On opening the abdomen the peritoneal surfaces are smooth

and glistening. There are a few adhesions about the appendix, and the neighboring fat contains considerable dense fibrous tissue.

The pericardial sac is normal.

The heart weighs 280 grams. The epicardium is smooth and glistening. The tricuspid and pulmonary valves are normal. The mitral valve is normal. The aortic leaflets are slightly thickened. There are few plaques of atheroma at the base of the aorta. The left ventricular wall measures 13 to 15 mm. in thickness. The myocardium is dark brown in color. The coronary arteries are normal.

The right lung weighs 330 grams. It lies free in the pleural cavity Its surface is translucent and glistening. The tissue is everywhere crepitant. The cut surface is pale. The structures at the hilum are normal.

FIG. 1.—Liver from Case I, showing marked cirrhosis and fibrous adhesions on surface.

The left lung is collapsed and is everywhere adherent to the thoracic wall and the diaphragm. The pleural covering of the lung is considerably thickened, especially along the posterior border, where it forms a dense, thick, white membrane. The left lung weighs 320 grams, with diaphragm attached. The tissue is resilient and contains very little air. The cut surface is dark red and hemorrhagic. The structures at the hilum are normal.

The spleen is greatly enlarged. It weighs 900 grams. It measures 22 x 15 x 8 cm. The surface of the spleen is pinkish red, smooth and glistening. The organ has a peculiar leathery consistence. Cut surface is pinkish red and oozes very little pulp. The Mal-

pighian bodies and trabeculæ are prominent. The splenic artery and vein are free from thrombi.

The liver (Fig. 1) weighs 400 grams. It is somewhat smaller than the normal, and very firm. The surface has a light grayish-brown color, and is coarsely granular, being traversed by irregular fissures of various depths. On the inferior surface of the liver the fissures are deeper than elsewhere, and divide the surface into a large number of nodules, varying from 0.1 to 2 cm. in diameter. Cut surface of the liver is light brown, opaque, and hob-nailed. The normal lobulation has been replaced by lobules of various sizes separated by translucent bands. The gall-bladder contains dark-brown viscid bile. The bile ducts are patent. There is no thrombosis of the portal vessels.

The pancreas is pale and firm. On section the lobules are easily separated. A few islands are visible. The pancreatic duct is patent. The lymph nodes surrounding the pancreas are enlarged.

The left kidney weighs 120 grams. The capsule strips easily, exposing a smooth pale surface. On section the cortical markings are distinctly seen, and pyramids are sharply defined.

The right kidney weighs 110 grams. It is similar to the left kidney in all respects. Pelves and ureters are normal. The suprarenal glands are normal. The bladder is normal.

The rectum contains dark, black, tarry material, evidently old blood. There are a few small dark-red irregularities on the mucosa, which have the appearance of partially healed ulcers.

The mesenteric lymph nodes are slightly enlarged.

The aorta is elastic, and there are a few plaques of atheroma.

The esophagus shows a few dilated veins.

The stomach is moderately dilated and contains dark-red fluid blood.

The gastric mucosa is dark red and glistening and mottled with small dark spots in many points. At no point, however, is there any visible break in the mucosa.

Duodenum contains dark brownish material. Jejunum and ileum contain dark-red coagulated blood. The mucosa of the small intestine is everywhere smooth and pale. The solitary follicles in the small gut are prominent. Attached to the head of the cecum there is some dense scar tissue which on section presents the appearance of a healed focus of some kind. Just below the ileocecal valve there are several small dark red projections on the surface of the mucosa which have the appearance of polyps. The large intestine is filled with black, tarry material. Except for the polyp-like structures, the mucosa of the large intestine is smooth and glistening.

Microscopic Examination. Spleen: There is considerable increase of interstitial tissue in both sinuses and follicles. The trabeculæ are much thickened and in places hyaline. In the interstices of the connective-tissue red-blood cells and leukocytes, chiefly of

lymphoid variety, occur in considerable numbers, The walls of the bloodvessels are much thickened, and there is considerable hyaline degeneration of the dense fibrous tissue around them. In many places red-blood cells show signs of disintegration.

FIG. 2.—Section of liver from Case I. (About 300 ×.) Marked intralobular proliferation of fibrous tissue with infiltration of lymphoid cells. At several points can be seen the ova of Schistosomum japonicum, some of them disintegrating.

Liver: There is a well-marked increase of connective tissue between the lobules (Fig. 2), especially along the courses of the portal vessels. The new-formed tissue is dense and infiltrated, with considerable numbers of lymphoid cells. There is some regeneration of small bile ducts. At many points in the interstices of the stroma there can be seen one or several sharply defined ova of some parasite; they are oval shaped and surrounded by thin refractile membranes, which may in turn be enclosed by foreign-body giant cells. A few of the ova have penetrated into the lobules, but the greater number lie in the interlobular tissue. Most of the ova are well preserved, and show extensive segmentation. A few, however, have been compressed and more are disintegrated by the fibrous tissue. One ovum is found completely surrounded by a calcareous capsule. The smaller arteries throughout the stroma show considerable thickening of the intimal coat. Except for some compression atrophy, the parenchymatous cells have not suffered.

Pancreas: There is no increase in the interstitial tissue. Islands of Langerhans are rather scarce.

Heart muscle is normal.

bosis. It is well-known that certain parasites secrete hemolytic substances and thus produce anemia, and that hematemesis may occur in any profound anemia. But certainly when the patient was first seen there was no degree of anemia sufficient to warrant such an interpretation of the symptoms. That toxins derived either from the parasites or their ova may directly excite such hemorrhages suggests itself, but such an explanation at present is purely hypothetical.

CASE II.—C. H., aged fifteen years, American, born in Japan; school-boy; admitted to hospital December 10, 1912, complaining of attacks of diarrhea, with bloody, mucous stools.

Previous Illnesses. None, except for one attack of pleurisy.

Present Illness. Five years ago the patient, who had been living in America for four years, went to China, arriving three in February. The following July he was taken acutely ill with chills and high fever. In a day or so large white blotches about one-eighth inch in diameter appeared over the abdomen, chest, and thighs, but none on the exposed body surface. They did not itch and were not painful or tender to touch. In about two weeks they disappeared. The diagnosis of the local physician was angioneurotic edema. The patient's fever, however, continued high in the evening and low or absent in the morning. There was moderate diarrhea, with more or less blood in the stools. The physician finally diagnosed the condition as typhoid fever. He was in bed six weeks and slight fever continued after he was up. During the winter the patient was much better, but had occasional attacks of diarrhea, with bloody stools. No vomiting at any time. The following spring he had a severe attack of diarrhea, with much blood in the stools, this attack lasting for six weeks. In July, 1908, he had chillls and fever again for three weeks, with the same bloody diarrhea. He was treated for malaria and also for the diarrhea, which persisted. During the entire following winter, at intervals of five or six weeks, he would have a hard chill followed by profuse sweats and high fever, and shortly after the chill the diarrhea would begin. The patient would go to bed for a day or so. Diarrhea would continue for three or four days and sometimes a week. There was no headache or pain with any of his attacks, except for slight cramps and griping pain in the bowels before a movement. The next spring the patient went swimming and waded much in stagnant ponds. One morning after he had been wading in the water for several hours, a profuse rash appeared on both legs from his knees to the ankles. The rash was in the form of bright-red pimples, about the size of a black-headed pin. The next morning the rash had disappeared. The following afternoon the patient was taken acutely ill with a hard chill, burning fever, and severe abdominal pain in the region of the appendix. Considerable abdominal distention and rigidity were present. Vomiting was so severe that he could

not retain water. There were frequent stools, composed chiefly of blood and mucus. On the following day the pain shifted to the left side, and then alternated from left to right. The abdomen continued distended and rigid. The severe abdominal pain and tenderness continued for three days, then gradually disappeared, but the fever, vomiting, distention and rigidity of lower abdomen with bloody, mucous stools continued for three weeks. The patient was in bed until the middle of September; was very weak and nervous; at times he was quite hysterical, and would cry for hours. The stools continued loose, and there was some blood in every movement. In the meantime the physician had examined the feces and found ova of the Schistosomum japonicum present. This examination was confirmed by Dr. Hume and other physicians of central China. The patient was given arsenic, which improved his nervous condition greatly. In October, 1910, he was brought to America and put under the care of Dr. Allan Smith, of Philadelphia, who advised outdoor life for him. He was on a farm all that winter and improved greatly, gained weight, grew in height, and his nervous condition was much better. At periods of four to six weeks, however, he was still subject to slight attacks of diarrhea, with blood and mucus in the stools. In the fall of 1911 he entered school in Princeton; his general condition was good, but there were still occasional attacks of diarrhea. During the past summer these became much less frequent. He has not had an attack now since September (three months). He has had no chills at all since coming to America. His general condition continues to improve. His mother says he has taken Blaud's pills for the past two years.

The patient comes to the hospital for examination and advice, anxious to know whether he is a source of danger to other students in the school.

Physical Examination. The patient is a well-developed young man, resting comfortably in bed, not in pain, of good color.

Superficial lymph nodes: Cervical, a few readily felt glands, not tender; axillary, a few just felt; right inguinal are moderately enlarged; left inguinal scarcely felt. Epitrochlear not felt.

Abdomen: Moderately full; soft; no tenderness; no masses; no rigidity.

Liver: Dulness from fifth space to costal margin in right mammary line. Edge is definitely felt 3 cm. below costal margin in right mammary line; not tender, seems firm and smooth.

Spleen: Percusses enlarged; edge is definitely felt one finger's breadth below costal margin in left mammary line; firm, not tender.

Surface: Brown "sun-burned" areas about the neck and arms. One small area 2 cm. x 1 cm. on right upper arm, scaling and slightly red.

Rectal Examination. The rectum contains a few hard fecal masses; there is no tenderness; no masses in wall of rectum; the

prostate is not enlarged or tender. Examination otherwise shows normal conditions.

December 10. Feces: A few ova of Schistosomum japonicum found. Faint reaction for blood.

December 11. Blood: Hemoglobin, 80 per cent.; red-blood cells 4,728,000. Differential leukocyte count: polynuclears, 81 per cent.; lymphocytes, 15 per cent.; large mononuclears, 2 per cent.; eosinophiles, 2 per cent.

Urine: 1030; acid; albumin, faint trace; glucose, none. Microscopic: a few white-blood cells; occasional hyaline casts; no blood.

December 17. A few ova of Schistosomum japonicum found in the feces.

December 19. Blood: Leukocytes, 19,100; polynuclears, 61 per cent.; lymphocytes, 18 per cent.; large mononuclears, 2 per cent.; eosinophiles, 19 per cent.

December 19. Patient discharged today; condition same as on admission. He has been up in a chair during a considerable part of his stay in the hospital. Temperature has varied from 98° to 100°. Pulse, 70 to 110.

The patient is advised to practise disinfection of his stools.

This case impressed upon us the possibility of the occurrence of this severe infection in Europeans and Americans living in the infected areas; it also suggested the desirability of publishing these reports, and, in view of the fact that this parasite has been known only since 1904, of gathering together all the facts regarding it to be obtained from the literature.

The African brother of this parasite, the Schistosomum hematobium, was discovered by Bilharz in 1851, who showed that it was the exciting agent in a disease of the genito-urinary tract since designated Bilharzia hematobia. This infection has come to be quite well known by reason of its widespread prevalence throughout Africa, Asia Minor, and Mauritius.

Historical Note (Manson). For some years Japanese physicians had observed in the provinces of Yamanashi and Hiroshima in central Japan and at Saga in the north island an endemic disease characterized by enlargement of the liver and spleen, cachexia and ascites. The patients suffered from diarrhea, their motions containing mucus tinged with blood. Occasionally they had fever. They became anemic, and many of them died of exhaustion. At autopsy the liver and other organs were found to contain the ova of some unknown helminth. As far back as 1888, Majima[2] in Tokio had found peculiar ova in the liver of a case of cirrhosis. These he described as the ova of an unknown parasite. In 1890, in a similar case, Yamigawa[3] found ova which he ascribed to the lung

[2] Manson's Tropical Diseases, fourth edition, p. 663.
[3] Virchow's Arch., 1908, cxciii, 325.

trematode. In April, 1904, Katsurada[4] discovered that the ova found in the stools of these patients contained a ciliated embryo not unlike the miracidium of Schistosomum hematobium.

Disappointed of an autopsy, he examined dogs and cats in the endemic area, and had at once the good fortune to discover in the portal systems of two cats from the province of Yamanashi numerous Schistosomata containing eggs exactly similar to those previously found in man. He published this information on August 13, 1904, and named the new trematode Schistosomum japonicum. Almost simultaneously and independently, Fujinami[5] observed cases of the disease in the village of Katayama in the province of Bingo, and found in his first fatal case the characteristic ova in various organs. In a second necropsy, besides the ova in the liver, intestinal wall, and mesenteric glands, he found in a branch of the portal vein a parasite which he regarded as Schistosomum hematobium. In November, 1904, Catto[6] discovered the same parasite in sections of the mesocolon of a Chinaman, from the province of Fukien, who died of cholera at St. John's Island, Quarantine Station, Singapore.

Geographical Distribution of the Parasite. Japan. Japanese writers (Tsuchiya) speak of the disease (schistosomiasis) as endemic in the provinces of Yamanashi, Hiroshima, and Saga. On account of the changing nomenclature of the Japanese provinces (employed by geographers) it is somewhat difficult to place these provinces accurately on modern maps, but Yamanashi and Hiroshima apparently belong to the extreme western part of the main island of the Japanese group, Hondu or Honshi, while Saga is to be found in the northern part of the adjacent islands of Kiusiu. Tsuchiya[7] also reports finding the eggs of the parasite in two Japanese from other parts of the country, one from the province of Miye and another who had passed his life in a village near Tokio.

China: Catto's original observation of the eggs of the parasite was made on the body of a Chinaman in Singapore. Beyer,[8] Peake,[9] Skinner,[10] Lambert,[11] and others report observations in a number of Chinamen in various parts of the Empire. Houghton,[12] in a comprehensive study of the disease in China, says that it has been shown to be endemic in the provinces of Hunan, Honan, Hupeh, Kiangsi, and Nganhui (Anhui), all of which lie in central China, along the valley of the great Yang-tse-Kiang. His own observations cover a territory of 100 miles about the city of Wuhu. Eight per cent. of all the males entering the Western General Hospital of that city are infected with this parasite, and in some parts 25 per cent. of the population suffer from diseases engendered by it.

[4] Manson's Tropical Diseases, fourth edition, p. 662.
[5] Trans. London Path. Soc., 1905, lvi, 179.
[6] Amer. Med., 1905, x, 578.
[7] Ibid., 1911, xiv, 129.
[8] Ibid.
[9] Loc. cit.
[10] Jour. Trop. Med., 1909, xii, 64.
[11] China Med. Jour., 1911, p. 308.
[12] Jour. Trop. Med., 1910, xiii, 185.

Philippine Islands: Wooley[13] discovered the infection in a native Filipino who had never been out of the islands and who at the time of his death was confined in the Bilbid prison.

England: Manson[14] found the ova of the schistosomum in the feces of a patient (presumably an Englishman) who has spent some time in north China, and speaks of it as the first observation of the infection in an European.

United States: Our own observations given above consitute, so far as can be learned, the first cases reported in this country. They were evidently both imported. Logan[15] reports the case of a boy, aged thirteen years, the son of an American missionary, who had probably suffered his infection while living at Yochow, Hunan. We are satisfied that our Case II is the same boy.

Description of the Parisite. Like the Schistosomum hematobium the Schistosomum japonicum is a bisexual trematode, the male measuring 9 to 12 mm. in length and 0.5 mm. in breadth; the female 12 mm. by 0.4 mm. The flat body of the male is folded over to form a gyneophoric canal, into which the body of the female is received. Both sexes bear upon the anterior extremity two suckers, a small one upon the very tip, a second, larger and pedunculated, being placed somewhat posteriorly upon the ventral surface. These suckers and the ventral surface of the body of the male are provided with minute spines. The body surface of the male is otherwise smoother than that of Schistosomum hematobium, and rather wider in the posterior part, the sides overlapping more extensively than in the latter. In further distinction from the Schistosomum hematobium, Catto[16] describes a larger vas deferens and lobulated testicles in the male Schistosomum japonicum, and a different arrangement of the yolk cells in the female. Looss[17] notes a greater development of the muscular system in Schistosomum japonicum, which he thinks may take the place of the cuticular eminences of Schistosomum hematobium.

The eggs, which occur in large numbers in the uterus of the female, measure on an average 0.055 mm. in length and 0.031 mm. in breadth. They are oval shaped, pale yellow, with thin refractile capsules, smooth surface, and contain either granular material or a developing embryo, the myracidium. The ova which are found in the feces nearly always contain myracidia, and are larger than the young undeveloped ova. The embryo as it lies in the ovum is pear-shaped, with a tapering trunk and sharp-pointed proboscis. Its average dimensions are 0.074 by 0.053 mm. It is made up of cells which contain refractile granules, and its surface is covered with cilia. If one of the eggs be pressed under a cover-glass, the parasite can be seen moving about inside the shell membrane.

[13] Filipine Jour. Science, 1906, i, 83.
[14] Jour. Trop Med., 1908, xi, 340.
[15] Ibid., 1911, xiv, 133.
[16] Loc. cit.
[17] Centralbl. f. Bakt., etc., 1905, 1 Abt., Orig., xxxix, 280.

The eggs of Schistosomum japonicum are to be distinguished from those of Schistosomum hematobium by the following differences

1. The ova of the former parasite are the smaller. Eggs of Schistosomum hematobium average 0.12 mm. x 0.05 mm., twice the dimensions of Schistosomum japonicum.

2. The ova of Schistosomum hematobium possess a lateral spine; those of Schistosomum japonicum do not. (R. T. Leiper[18] has recently published a note in which he claims to have demonstrated small knob-like spines on the ova of Schistosomum japonicum.)

PATHOGENESIS. The disease occurs almost exclusively among workers in rice fields and among children who bathe in the canals adjoining rice fields. In June the fields are flooded with water from the canals and then manure (human feces)—the chief source of infection—is spread over the soil. People working in the fields at this time are often taken with an unpleasant itching and rash on the parts of the body exposed to the water. Observation of these facts soon led Japanese investigators to the conclusion that the portal of entry of the infection was usually, if not always, to be found in the skin, and experiments have shown that in the case of animals, at least, infection through the skin is much more easily accomplished than infection by way of the digestive tract. Fujinami and Nakamura[19] kept six healthy calves standing for several hours in flooded rice fields, with bandages over their mouths. In the control series, the legs of the calves were wrapped with oil-cloth and no gags were placed over the mouths. All six of the calves whose legs had been exposed, became infected with the Schistosomum japonicum, while in the control series only one showed the parasite and this one had only two foci. Similar experiments were performed with dogs and rabbits. Katsurada and Hashegawa[20] carried out some ingenious experiments on cats and pups. Wooden yokes were placed about their necks so as to render infection per os impossible; then the animals were put in the flooded rice fields or in the canal water. In this way they were easily infected. Attempts, however, to transmit the disease by giving them infected water proved futile. Katsurada and Hashegawa concluded from their experiments that infection with Schistosomum japonicum takes place solely by way of the skin. The fact that the miracidia are soon killed by 0.1 per cent. hydrochloric acid supports this view, as it makes infection through the stomach practically impossible.

Fujinami and Nakamura were unable to determine whether the parasite entered the skin in the form of the miracidium itself or whether an intermediate host was necessary for infection. More recently, however, Matsuura and Yamamoto[21] demonstrated a Schistosomum japonicum larva just entering the skin, and a few

[18] Jour. Trop. Med., 1911, xiv, 76.
[19] Kyoto igakn Zassi, vi, Fasc. 4.
[20] Centralbl. f. Bakt. etc., 1910, I Abt. Orig., liii, 519.
[21] Chugai Iai Shimpo, 1911, p. 755.

days later found larvæ similar in size and structure in the infecting water.

Location and Distribution of the Parasite in the Body. The parasite having gained entrance to the body finally takes up its abode in the portal vein and its branches. Tsuchiya[22] found the parasites only in the portal vein in careful examinations made in seven cats, one dog and three men. In all 410 parasites, about equally divided between male and female, were recovered from the seven cats. Of these 150 were paired, the remainder single. Nearly all the parasites found in the mesenteric veins were in copulation, while in the portal vein or its branches many single individuals were found. Tsuchiya thinks that sexually immature parasites or those unable to find a mate remain in the portal vein or its branches in the liver; but that the copulating parasites make their way back against the blood-stream into the mesenteric veins and finally to the intestinal tract, where the eggs are deposited in the smaller vessels and capillaries. The ova do not, as a rule, remain in the capillaries, but wander out into the stroma of the mucosa and submucosa of the stomach and intestine. Here they collect in large numbers and many of them eventually break through the mucous membrane (with the production of more or less ulceration) and become mixed with the intestinal contents. The ova that remain in the tissue are attacked by leukocytes and destroyed, or they become encapsulated with fibrous tissue and undergo calcareous degeneration. Some of the ova are carried by the blood into the liver and become lodged in the capillaries there. Others find their way into the mesenteric lymph glands.

Pathology. The most constant and characteristic gross findings in Schistosomum japonicum infections are enlargement of the liver, spleen, and mesenteric lymph glands. In the later stages of the disease the liver may be small and hard, due to destruction of the parenchyma and contraction of the fibrous tissue. In either case the liver is quite firm and resistant; its surface is coarsely granular or nodular (Fig. 1), suggesting syphilitic cirrhosis. The older the infection the more advanced the cirrhosis. The cut surface is coarsely granular, pale yellow, and traversed in every direction by dense bands of fibrous tissue, which appear to follow the portal vessels.

Microscopically the liver shows more or less extensive new growth of fibrous tissue (Fig. 2), particularly about the portal vessels. In the meshes of the stroma the eggs of Schistosomum japonicum are found, sometimes well preserved, at other times compressed and atrophied. In the earlier stages of the disease there is considerable infiltration of lymphoid cells about the ova.

The spleen is hypertrophied, usually considerably so, and very

[22] Loc. cit.

firm in consistence. This increase in size and consistence is due to the portal congestion and consequent proliferation of fibrous tissue. The cut surface is dark red, and oozes a small amount of pulp.

Microscopic sections show a partial replacement of the follicles by connective tissue, which has also filled up the sinuses. The trabeculæ are greatly thickened, and may show hyaline degeneration. The mesenteric lymph glands are enlarged, and sections show changes similar to those observed in the spleen. Here and there in the fibrous tissue or lying free in the sinuses are found ova of Schistosomum japonicum.

The pathological changes in the gastro-intestinal tract are most marked in the lower portion of the small gut and the whole of the large intestine. In the gross the lesions are often not striking. In the milder cases the mucosa may show nothing more than numerous minute punctate hemorrhages of a reddish brown color. In the severer cases, hemorrhagic ulcers of various sizes occur. The mucosa becomes hypertrophied and thrown up into folds, so that in some places small polyps are formed. The serosa, especially that of the large gut, may become thickened and bound to the other viscera by fibrous adhesions. Microscopically the lesion is the same throughout the gastro-intestinal tract, varying, however, in severity. The characteristic lesion consists of a deposit of ova in the submucosa (Fig. 3), which lie embedded in granulation tissue if recently deposited, or dense fibrous tissue if of long duration. The mucosa may be intact, but more often there is atrophy, or complete destruction of the mucosa, with the formation of ulcers. The dilated veins of the submucosa give these a hemorrhagic quality. The muscularis is usually free from invasion, but the serosa often contains deposits of eggs, which produce chronic inflammatory changes and thickening of the fibrous coat.

As intimated above, the lower portion of the ileum and the entire large intestine are chiefly affected, but small groups of ova are sometimes found in the wall of the stomach, duodenum, and jejunum In addition to these more usual locations ova are occasionally found in the lungs, spleen, pancreas, mesentery, gall-bladder, and brain (Yamagiwa).

Symptoms. These may be explained as in part the results of mechanical irritation produced by the presence of the eggs of the parasite in the intestinal mucosa or other parts, such as the spleen and liver, in part the results of a hemolytic secretion of the parasites (Yagi[23]), or in the terminal stages as the results of both factors. It is obvious that as in other parasitic invasions, Ankylostomum duodenale or Schistosoma hematobium, for example, infection by the Schistosomum japonicum may occur without resulting symp-

[23] Arch. f. exper. Path. u. Pharm., 1910, lxii, 156.

toms. Manson[24] reports his finding in a patient who had only vague digestive disturbances. In our first case it is doubtful whether the ova had anything to do with the hematemesis from which the patient died. From the mild or latent infections varying grades of disturbance up to severe dysentery, anemia, enlargement of liver and spleen, ascites, and fever may be seen. Houghton,[25] who has had unusual opportunities to observe the disease, classifies the cases clinically as follows:

1. Cases showing ova in stools but no bodily reaction—2 out of 40 cases.

2. Cases negative except for marked eosinophilia. These, he says, make bad surgical risks.

3. Cases presenting only splenic enlargement. These are often difficult to diagnose, if the ova are absent or scarce in the stools. An eosinophilia of over 10 per cent. he regards as suggestive—11 out of 40 cases.

4. Cases with cerebral symptoms and a high grade of eosinophilia. He had only a single case of this type, and there is no proof that the schistosomum infection was in any way related to the hemiplegia from which the patient suffered, although Yamagiwa[26] reports that he found the ova of Schistosomum japonicum in the cerebral cortex of a patient who had suffered from Jacksonian epilepsy. Tsuchiya,[27] in two of his autopsies, found the eggs in the lungs and pleura. Usually the parasites and their eggs are confined to the portal system, but it is obvious that if the eggs reach the lungs, they may be carried to the brain, and, lodging there, may produce symptoms.

5. Typical cases showing enlargement of the liver and spleen, dysentery (with bloody stools)—16 out of 40 cases. In this group our second case would belong. The recurrent fever with which our patient suffered is noteworthy. Such fever may be the first symptom of the disease, and only after the fever has run for some time may the other symptoms develop (Tsuchiya.)

To these groups should be added:

6. Terminal cases in which in addition to the symptoms of the preceding group the patients present evidences of portal obstruction (ascites) and advanced anemia, and die of exhaustion. One of Tsuchiya's patients had had his abdomen punctured forty-eight times in the course of three years. The ascites may be explained partly by the cirrhosis of the liver, partly by an endophlebitis and thrombosis of the veins of the portal system, excited by the eggs of the parasites. In man the parasites seem not to be present in sufficient number to directly affect of themselves the circulation of the portal system. Jaundice may be present in this stage of the disease, but appears to be a relatively rare symptom.

[24] Loc. cit.
[25] Loc. cit.
[26] Virchow's Archiv, cxix, 447.
[27] Loc. cit.

INDIVIDUAL SYMPTOMS. *Skin Eruptions.* The cutaneous phenomena described in the history of our second patient give rise to interesting questions. Have they any relation to the infection from which he was later proved to be suffering? Do they represent the results of irritation produced by the larvæ of the schistosomum? In this connection we recall with interest the observation of the prevalence of ground-itch in hook worm districts by Bentley, the occurrence of a dermatitis on Loos' hands on exposure of the skin to "cultures" of the ankylostomum larvæ, and his subsequent demonstration that these larvæ can pass the skin and ultimately by this route reach the intestinal tract. In Porto Rico, Ashford, King, and Gutierrez found that 98 per cent. of patients suffering from ankylostomum infection gave a history of the characteristic dermatitis or "mazamorro" as the natives name the affection. Skin infection has come to be accepted as at least the common path of infection in this disease, and there is, as already shown, evidence that the like situation prevails with relation to the schistosomum.

The phenomena in our patient diagnosed as angioneurotic edema appear to have had much too general a distribution to warrant the belief that they could have been caused directly (by irritation produced) by larvæ of the parasite unless the patient had been bathing in badly infected water. Of this there was no history. On the other hand the rash on the legs and arms later described developed after the symptoms of his affection had been present for more than a year, and the illness which followed developed too promptly to allow one to regard it as possibly a new infection. The possibilities presented by the skin phenomena in this case can at present be regarded only as speculations. Nowhere in the literature have we found any extended reference to such skin eruptions. Matsura and Yamamoto[28] have, however, shown that the larva of Schistosomum japonicum may be found entering the skin and have demonstrated the presence of like objects in infected water. Lambert describes the case of a sportsman who suffered from low fever, with urticaria and a high eosinophilia, in whose stools he later found the ova of Schistosomum japonicum. He states his conviction that the disease occurring in the Yangtse Valley and known locally as river fever, urticarial fever, or Yangtse fever are all one and the same infection by this parasite. His remarks imply that urticaria is a common occurrence (or urticaria together with fever) in the early stages of the disease, but he does not give the details of his observations.

CIRCULATORY SYSTEM. In the later stages of the disease, edema of the ankles or a general anasarca may develop as a sequel of advanced anemia and exhaustion, but the heart and major circulation are not usually affected, and in the early stages of the disease

[28] Loc. cit.

present only such disturbances as belong to the fever and exhaustion produced by the infection.

Respiratory System. As in our first patient, Tsuchyia[29] found dense pleural adhesions and thickening of the pleura at autopsy. He also demonstrated hemorrhagic infarction of the lung near which individual eggs of the parasite could be found, but not in such relation as to indicate that the infarction had resulted from their presence. He, therefore, regarded it as resulting from hypostatic congestion in the terminal stage of the disease.

Alimentary Tract. In the nature of things the symptoms are mainly referred to this tract, and they may be very mild, as in Manson's patient, or so severe as to end in death.

Diarrhea is a fairly constant feature of the clinical picture. In the milder cases the diarrhea is slight, the stools are watery or soft; in the severer conditions the diarrhea is distressing, the stools containing mucus and blood. Bleeding from the bowel may be so severe as to be the cause of death. We can, however, find no reference to such an experience as we had with our first patient.

Enlargement of the liver and spleen occurs early in the disease, and appears to persist throughout. The enlargement is gradual and painless. The surface of the liver, originally smooth, may later show irregularities due to cicatricial contraction. The spleen is large, firm, and sharp-edged. Jaundice is a rare complication.

Ascites is a late development resulting from portal obstruction. It may be evanescent, disappearing in some instances after one tapping; in other cases persisting after more than forty. With ascites the veins of the abdomen may be enlarged, but they are rarely as prominent as in atrophic cirrhosis of the liver.

The enlargement of the spleen may be very marked. It occurs quite independently of the presence of parasites or eggs in the spleen itself. In the late stages of the disease it is largely due to portal congestion, and may be greatly reduced, as in our first case, by a large hemorrhage (Tsuchiya.)

Urinary System. The urine shows no changes characteristic of the disease. The ova of Schistosomum japonicum never appear in the urine.

Blood. The changes in the blood are important. By some writers anemia is spoken of as a characteristic feature of the disease. It is evident that if bleeding from the alimentary tract be persistent, progressive anemia must follow. Houghton and others, however, speak of anemia as rather an infrequent result of the infection. Eosinophilia appears to be almost constantly present, as in infection with other parasites. Lambert[30] says that the eosinophilia may amount to 60 per cent. of the leukocytes. The leukocytes may be, but are commonly not, increased in total number. In anemia

[29] Loc. cit. [30] Loc. cit.

the red blood cells and hemoglobin are both reduced, but the latter to a greater degree, as in any secondary anemia.

DIAGNOSIS. In the districts where the disease is endemic Lambert asserts that the diagnosis can be made before the appearance of ova in the stools on the following points:

1. A history of bathing or wading in shallow ponds or rivers in the vicinity of the Yangtse River, followed, if only one prolonged contact with infected water has occurred, by:
2. An incubation period of ten to fifteen days.
3. Fever 100° to 102° and sweating.
4. An eosinophilia possibly amounting to 60 per cent.

It is quite evident that while these points may suffice to identify the affection under special conditions, they cannot be relied upon to do so at all times. Apart from the history of exposure to infected water the phenomena would suggest trichinosis quite as strongly as infection with the Schistosomum. If the antigen were more easily obtained, the complement fixation reaction could be employed, for Yoshimoto[31] has shown that it affords an accurate means of diagnosing Schistosomiasis.

The only conclusive clinical evidence of this infection must be the finding of the ova in the stools. The points of distinction of these have already been given. They are almost identical with the ova of Schistosomum hematobium, but may be differentiated from them by their smaller size and the absence of the lateral spine.

The ova are usually found without much difficulty, though in our second case some specimens of feces failed to show any. We made the observation that ova were more numerous in stools that contained blood than in those that were free from it.

PROGNOSIS. As to life, prognosis is good; as to health, bad. No exact statistics of mortality are available. Katsuura says that he had seen from 30 to 54 cases in each of five years, and of these numbers from 3 to 5 would prove fatal. He thought it probable that the indirect mortality of the disease would be much higher.

The duration of life varies greatly. In the worst cases it appears to be several years before the patients succumb. Under more favorable conditions life may be protracted twenty to thirty years. Two of Tsuchiya's patients were between sixty and seventy years of age; one had led an active life for thirty years after the onset of symptoms.

In fatal cases death resulted either from exhaustion consequent to persistent ascites and repeated paracentesis, or hemorrhage, or complications induced by the increased abdominal pressure.

PROPHYLAXIS The evidence at present is that the miracidium is the dangerous form of the parasite. If its development is checked, or its ingress into the skin prevented, infection fails. The important

[31] Zeitsch. f. Immunitätsf., etc., 1910, Orig., v, 438.

steps, therefore, appear to be the prevention of the access of the miracidium to fresh water or the contact of infected water with the human skin. How difficult these steps may be in such districts as the Yangtse Valley appears at once, when we learn that all through China and Japan fresh human feces is used as fertilizer, and that thousands of people who make their living as fishermen, lumbermen, boatmen, etc., as well as those who occasionally wade or bathe in lakes or rivers, are exposed to infection.

Yet the situation is not entirely hopeless. There is evidence that if prevented from reaching fresh water even for a few days the miracidium dies and the danger of infection ceases. The general adoption of water-tight latrines or vaults in which the feces could be retained for a time would meet the requirements of the situation. Of course, the proper disinfection of the feces by formaldehyde, lime, or any other active disinfectant would also be effective, but such measures are practically useless among a population innocent of all knowledge of sanitation.

For the European the important point appears to be the avoidance of bathing or wading in shallow streams, lakes or ponds in the infested district. Doubtless there is some danger in exposure of the skin to any untreated water, but this appears to be remote except under the special conditions noted.

The full explanation of these facts in the life-history of the miracidium has not yet been worked out. Under conditions of life in this country there appears to be very little danger of the spread of infection. Yet the possibility cannot be denied, if the discharges of infected persons are allowed to contaminate small streams, in which other persons bathe or wade. Disinfection of the stools of every one known to be suffering from the disease must therefore be required.

Since the exact route of infection is still a moot question, it goes without saying that all persons living in an area where schistosomiasis is endemic should drink only carefully filtered or boiled water.

TREATMENT. Removal from the zone of danger is advised, as this will at least prevent reinfection. It is believed that in time the parasites die out, the eggs are evacuated or encysted, and if the patient survives the disease becomes quiescent. Diarrhea within certain limits is not harmful, but rather a method of elimination. Our efforts, therefore, must be directed toward careful feeding to prevent loss of weight and strength, the administration of iron to correct the anemia, and such general tonics as may be indicated. If ascites develops, tapping relieves it, and it may not return. In the earlier stages it may be met by restriction of fluids, a low-salt diet and saline catharsis, as in cirrhosis of the liver.

THE ABSENCE OF HYPERPLASIA OF THE REMAINDER OF THE THYROID IN DOGS AFTER PIECEMEAL REMOVAL OF THIS GLAND. AUTO-TRANSPLANTATION OF THE THYROID IN PARTIALLY THYREOIDECTOMIZED ANIMALS.

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I would here express my thanks to Dr. Halsted,[1] at whose suggestion these experiments were conducted.

Dr. Halsted in 1887 and 1888 showed that in dogs hypertrophy took place in the remaining gland after small pieces of a lobe had been removed.

In the experiments which follow, the manner in which the wounds healed did not seem to affect in any way the behavior of the remainder of the thyroid in the necks of the dogs.

The operation of piecemeal removal was performed on 39 dogs, and the wounds, with few exceptions, healed absolutely *per primam*. Only in one of these 39 dogs did the remainder of the thyroid present a picture of marked glandular hyperplasia.

In 20 dogs the wounds were left open to heal with suppuration. Neither hyperplasia nor hypertrophy were observed in the remaining thyroids of these dogs. Hypertrophy is used to denote measureable increase in the size of the remaining thyroid; hyperplasia signifies changes in the histological picture.

The Effect upon the Remaining Gland in the 39 Dogs of the Aseptic Series, Table 1. Dogs 1 to 11; 101 to 124; 501; 701 to 703. In this series the pieces removed at the first operation varied in size. The largest amount removed at the first operation was one and three-quarter lobes; the smallest was approximately one-fifth of one lobe.

In dogs Nos. 120, 121, 123, 124, and 501 no transplantations were made at the first operation; in the remaining 34 dogs autotransplantation was the invariable rule at the first operation.

Of 36 dogs only 3 of the pieces obtained at the second operation or at autopsy differed microscopically from the pieces removed at the first operation. In these three dogs the change was from early glandular hyperplasia to normal.

[1] Dr. Halsted in a paper on Reconsideration of the Question of Experimental Hypertrophy of the Thyroid Gland, and the Effect of Excision of this Organ upon Other of the Ductless Glands, delivered before the Congress of Physicians and Surgeons, Washington, May, 1913, alluded to the experiments which are herewith reported. See Amer. Jour. Med. Sci., 1914, No. 1, vol. clxvii, p. 58 and 59.

Dog No. 1. The inferior fourth of the left lobe removed at the first operation showed early glandular hyperplasia. The piece removed 81 days later at the second operation was normal.

Dog No. 9. The inferior one-fourth of the left lobe removed at the first operation showed early glandular hyperplasia. The piece removed 66 days later at the second operaation was normal.

Dog No. 102. The inferior one-fourth of the left lobe and the inferior two-fifths of the right lobe removed at the first operation showed early glandular hyperplasia. The pieces obtained when the animal was sacrificed 94 days after the first operation were found to be normal.

There was no change in the structure of the remaining gland in 33 dogs during the intervals between the first and second operation or autopsy. The intervals between the first and second removals were: 41, 41, 62, 64, 30, 42, 84, 66, 96, 114, 21, 21, 61, 50, 22, 30, 15, 16, 21, 83, 84, 75, 23, 59, 57, 30, 23, 20, 20, 34, 87, 33, and 62 days.

The specimens removed from the following three dogs at the first operation were lost.

Dog No. 109. The pieces obtained at autopsy 24 days after the first operation were normal in structure. Amount of privation at the first operation was one lobe.

Dog No. 118. One and one-third lobes removed at first operation. Piece removed 58 days after first operation was normal.

Dog No. 122. Two-thirds of one lobe removed at first operation. Piece removed 153 days after first operation was normal.

The remaining glands in 18 dogs did not undergo a change in size or structure during the intervals between the second and third operations, or during the intervals between the second operations and autopsies. The intervals between the second and third operations or autopsies were: 71, 105, 129, 95, 80, 85, 63, 94, 84, 51, 42, 54, 55, 24, 54, 25, 12, and 25 days.

In one dog the remaining gland removed at the third operation showed a structural change:

Dog No. 114. The inferior fifth of the right lobe removed at the first operation was normal. At operation II, 84 days after first operation, the entire left lobe and one-half of the remaining four-fifths of the right lobe were removed. Total privation, one and three-fifths lobes. The pieces removed at the second operation were normal. The remaining two-fifths of the right lobe removed when the animal was sacrificed 53 days after the second operation, 137 days after the first operation, had not increased in size, but on examination presented a picture of marked glandular hyperplasia.

The small piece of one lobe remaining to each of 8 dogs at the fourth operation had, with two exceptions, undergone no change in size or structure.

In six dogs (Nos. 1, 2, 3, 4, 5, and 7) the pieces obtained at the

fourth operation presented the same histological picture as those from the third operation. The intervals between the third and fourth operations were: 98, 104, 79, 91, 101 and 58 days. The total number of days between the first and fourth operations on these dogs were: 250, 251, 249, 248, 245, and 185 days.

Dog No. 1. Operation I. Deprived of one-fourth of left lobe. Diagnosis: early glandular hyperplasia. Operation II, eighty-one days after the first, deprived of remaining three-fourths of left lobe. Diagnosis: normal. Operation III, seventy-one days after second, and 152 days after first operation, deprived of two-thirds of the right lobe. Diagnosis: normal. Total privation now one and two-thirds lobes. Operation IV, 98 days after third and 250 days after the first operation. Remaining one-third of right lobe removed. Diagnosis: normal.

Dog No. 2. Operation I. Inferior one-third of left lobe removed. Diagnosis: normal. Operation II, 41 days after first, remaining two-thirds of left lobe and the inferior one-fifth of right lobe removed. Diagnosis: normal. Total privation, one and one-fifth lobes. Operation III, 105 days after the second and 146 days after the first operation, two-thirds of the remaining four-fifths of the right lobe removed. Total privation, one and eleven-fifteenth lobes. Diagnosis: normal. Operation IV, 104 days after the third and 250 days after the first operation, the remaining four-fifteenths of right lobe removed. Diagnosis: normal.

Dog No. 3. Operation I. Inferior one-half of left lobe removed. Diagnosis: normal. Operation II, 41 days after first, the remaining one-half of left lobe and the inferior one-half of right lobe removed. Diagnosis: normal. Amount of privation, one and one-half lobes. Operation III, 129 days after the second and 170 days after the first operation. One-third of the remaining one-half of right lobe removed. Amount of privation, one and two-thirds lobes. Diagnosis: normal. Operation IV, 79 days after the third and 249 days after the first operation. The remaining one-third of right lobe removed. Diagnosis: normal.

Dog No. 4. Operation I. Entire left lobe removed. Diagnosis: normal. Operation II, 62 days after the first. Inferior one-fifth of right lobe removed. Diagnosis: normal. Amount of privation, one and one-fifth lobes. Operation III, 95 days after the second and 157 days after the first operation. One-third of the remaining four-fifth of the right lobe removed. Diagnosis: normal. Amount or privation, one and seven-fifteenths lobes. Operation IV, 91 days after the third and 248 days after the first operation. Remaining eight-fifteenths of right lobe removed. Diagnosis: normal.

Dog No. 5. Operation I. Inferior half of left lobe removed. Diagnosis: normal. Operation II, 64 days after the first. The remaining one-half of left and one-half of the right lobe removed. Diagnosis: normal. Amount of privation, one and one-half lobes.

Operation III, 80 days after the second, 144 days after the first operation. One-third of the remaining one-half of right lobe removed. Diagnosis: normal. Amount of privation, one and two-thirds lobes. Operation IV, 101 days after the third and 245 days after the first operation. The remaining one-third of right lobe removed. Diagnosis: normal.

Dog No. 7. Operation I. Entire left lobe removed. Diagnosis: early glandular hyperplasia. Operation II, 42 days after the first. Inferior one-fourth of right lobe removed. Diagnosis: early glandular hyperplasia. Amount of privation, one and one-fourth lobes. Operation III, 85 days after the second and 127 days after the first operation; one-half of the remaining three-fourths of the right lobe removed. Diagnosis: early glandular hyperplasia. Amount of privation, one and five-eighths lobes. Operation IV, 58 days after the third and 185 days after the first operation. Remaining three-eighth of right lobe removed. Diagnosis: early glandular hyperplasia.

The remaining gland in two dogs (Nos. 9 and 11) showed a structural change at the fourth operations; a change from normal to early glandular hyperplasia.

Dog No. 9. Operation I. Inferior one-fourth of left lobe removed. Diagnosis: normal. Operation II, 66 days after the first operation. Remaining three-fourths of left lobe and one-third of right lobe were removed. Diagnosis: normal. Amount of privation, one and one-third lobes. Operation III, 94 days after the second and 160 days after the first operation. Two-thirds of the remaining two-thirds of right lobe removed. Diagnosis: normal. Amount of privation, one and seven-ninths lobes. Operation IV, 76 days after the third operation and 236 days after the first. Remaining two-ninth of right lobe removed. Diagnosis: very early glandular hyperplasia.

Dog No. 11. Operation I. Inferior one-third of left and inferior one-third of right lobe removed. Diagnosis: normal. Operation II, 96 days after the first operation. The remaining two-thirds of the right lobe and one-fourth of the remaining two-thirds of the right lobe removed. Diagnosis: normal. Amount of privation, one and one-half lobes. Operation III, 51 days after the second and 147 days after the first operation; one-fifth of the remaining one-half of right lobe removed. Diagnosis: normal. Amount of privation, one and three-fifths lobes. Operation IV, 39 days after the third and 186 days after the first operation. The remaining two-fifths of right lobe removed. Diagnosis: very early glandular hyperplasia.

BEHAVIOR OF THE REMAINING GLAND IN DOGS WHOSE NECK WOUNDS WERE LEFT OPEN AND HEALED WITH SUPPURATION. Table II. Dogs 301 to 320. The operation of piecemeal removal was performed by cutting through hair and skin, observing no

aseptic precautions and leaving the wound open. All of the cervical wounds in the dogs of this series healed with suppuration.

In this series of 20 dogs, the pieces removed at the first operations were diagnosed as follows: normal, 9; very early glandular hyperplasia, 2; early glandular hyperplasia, 7; marked glandular hyperplasia, 2.

The sizes of the pieces removed at the first operation varied from one-fifth of one lobe to one and five-twelfths lobes. The longest interval between the first and second removals was 58 days; the shortest interval 10 days. The diagnoses of the respective pieces removed at the second operation were the same as the diagnoses of the pieces removed at the first operation on the same dogs, except in two cases.

Dog No. 311. Operation I. Left lobe removed. Diagnosis: early glandular hyperplasia. At autopsy 31 days later the remaining right lobe was found to be normal in structure.

Dog No. 314. Diagnosis of left lobe removed at first operation: early glandular hyperplasia. Diagnosis of the remaining right lobe removed 50 days after first operation: normal.

No change in size or structure was observed in the pieces of the remaining glands from 18 dogs removed at the second operation. The intervals between the first and second operations were: 40, 10, 41, 14, 29, 37, 18, 22, 49, 42, 11, 50, 45, 26, 52, 52, 58, and 52 days.

In dog No. 301, a piece of the remaining left lobe removed at the third operation, 90 days after the first, showed no change in structure or size.

In Dog No. 303 (58 days' interval between the first operation and sacrifice of the dog), the remaining one-half of right lobe showed no change in structure or size.

In Dog No. 306 (76 days' interval between the first operation and sacrifice of the animal), the remaining right lobe showed no change in size or structure.

Dog No. 319 gave birth to five puppies 54 days after one and five-twelfths lobes had been removed. The remaining seven-twelfths of the right lobe, obtained when the animal was sacrificed 4 days after delivery, showed no change in size or structure. Diagnosis of pieces first removed: normal. Diagnosis of pieces obtained when the dog was sacrificed 58 days after the first operation normal.

AUTOTRANSPLANTATION OF THE THYROID GLAND.

Of forty-two transplantations, nineteen were successful. The amount of privation of thyroid gland in the animals yielding the living graft varied from one-fifth of one lobe to one and seven-ninths lobes.

Two-thirds of one lobe were removed from dog No. 11, and a portion of this piece was transplanted at the same operation. The graft was not removed at the second operation nor at the third, when the gland in the neck was reduced in amount to four-fifteenths of one lobe. The graft was obtained at the fourth operation when it had been in the abdominal cavity wall for six months; it had changed from normal to very early glandular hyperplasia. The four-fifteenths of the one remaining lobe in the neck of this dog had undergone the same change.

The oldest graft was obtained from dog No. 9, approximately seven and one-half months after implantation and had changed from normal to very early glandular hyperplasia. The thyroid in the neck had been reduced from one and three-fourths lobes to two-ninths of one lobe.

Two implantations were made into dog No. 122 at the first operation when two-thirds of one lobe had been removed. These grafts were recovered five months and twenty-five days after implantation, when there remained to the dog only two-thirds of one thyroid lobe.

The transplantation of round cylinder-shaped pieces of gland, obtained by using a sharp punch, gave the most convincing results. These pieces of gland were uniform in size and measured 5 x 4 mm.

Grafts at body temperature placed into freshly made pockets which contained no blood yielded the best results. After cutting through the anterior sheath of the rectus abdominis muscle, the median border of the muscle was pushed aside and a pocket made by opening and closing the jaws of a fine-pointed artery clamp. Great care was taken to maintain a bloodless dissection.

THE EFFECT OF AUTOTRANSPLANTATIONS UPON THE CERVICAL THYROIDS.

No transplantations were made in the 20 dogs of the series in which no antiseptic precautions were observed. Table II, dogs 301 to 320. Not in one of these dogs did the remaining gland undergo a structural change after pieces of various sizes had been removed.

No transplantations were made in 5 dogs of the aseptic series: Nos. 120, 121, 123, 124, and 501. The intervals between the first operations and autopsies were 30, 23, 20, 20, and 34 days. The control specimens removed at the first operations in these dogs were the same structurally as the pieces obtained when the animals were sacrificed.

In 23 dogs the grafted tissue was absorbed.

The greater part of the one-fourth of the left lobe removed from dog No. 1 at the first operation was transplanted. This graft had

been completely absorbed when searched for at the second operation 81 days after the first. A greater part of the remaining three-fourths of the left lobe was transplanted at the second operation. This graft when searched for 169 days after implantation could not be found.

Dog No. 2. A greater part of the remaining two-thirds of the right lobe removed at the second operation was transplanted. The graft when searched for at the fourth operation 209 days after the second had been absorbed.

Dog No. 3. Graft transplanted at first operation and searched for at the second operation 41 days after the first had been absorbed. Operation II. No transplantation. Operation III. A small piece of the piece removed from the remaining one-half of the right lobe was transplanted. This graft, 79 days later, had been etirely replaced by connective tissue.

Dog No. 4. The three transplants were absorbed. They were searched for 62, 95, and 91 days after implantation.

Dog No. 5. Greater part of the one-half of the left lobe removed at the first operation was transplanted. Operation II, 64 days after the first. No trace of graft. Greater part of one-half of right lobe transplanted. Operation III, 80 days after the second. Graft replaced by connective tissue.

The control specimens of thyroids removed from 10 dogs at the first operations were hyperplastic (dogs Nos. 1, 7, 9, 10, 101, 102, 105, 110, 113, and 701). Transplantation was the rule at the first operations on these dogs with hyperplasic glands. In 3 of the 10 dogs the remaining thyroid in the neck of the animals changed from the hyperplastic type to normal. The grafts in 2 of the 3 dogs were absorbed, while in the third a living graft was obtained when the dog was sacrificed (Dog No. 9). In 7 of the 10 dogs the grafts were absorbed, except in one case, dog No. 113. The graft in this dog was in a perfect state of preservation when removed 137 days after implantation. There was no change in the grade of hyperplasia in the remaining cervical thyroids of the 7 dogs in question, hyperplastic at the first and last removals.

Two experiments (dogs Nos. 9 and 11) tend to show that the grafted thyroid undergoes a change in structure similar to the change in the remaining thyroid in the neck of the dog.

Dog No. 9. Two grafts in this dog changed from normal to very early glandular hyperplasia during the interval between the third and fourth operations. The remaining two-ninths of the right lobe underwent the same change.

Dog No. 11. The remaining two-fifths of the right lobe and the graft in this dog changed from normal to very early glandular hyperplasia during the interval between the third and fourth operations.

THE ACCESSORY THYROIDS IN DOGS PARTIALLY DEPRIVED OF THE THYROID GLAND.

Accessory thyroid glands were searched for and found in dogs 9, 11, 101, 113, 114, 118, 306, 318, 230, and 701. The accessory thyroids always presented precisely the same histological picture as the remains of the thyroid gland in the neck.

SUMMARY.

1. One and three-fourths of the dog's thyroid gland may be removed without appreciably affecting the remainder of the gland.
2. In only 3 of the 59 dogs on which the operation of piecemeal removal was performed did the remaining gland change from a normal to a hyperplastic state. Dogs Nos. 9, 11, and 114.
3. In 5 of the 59 dogs the remaining gland reverted from the early hyperplastic state to the normal state. Dogs Nos. 1, 9, 102, 311, and 314.
4. Where a diagnosis of some degree of hyperplasia was made at the first operation, the pieces removed from the same dogs at subsequent operations had not undergone further hyperplasia.
5. Of the pieces removed from 56 dogs at the first operation, 58 per cent. were normal, 32 per cent. showed early glandular hyperplasia, 5 per cent. marked glandular hyperplasia, and 5 per cent. very early glandular hyperplasia.
6. Definite increase in the size of the remaining gland (hypertrophy) was not observed.
7. The remains of the thyroid lobes, the accessory thyroids, and the successful grafts in a given dog, presented the same histological picture.
8. In no dog was myxedema or tetany observed in which as much as one-fourth of the thyroid and one parathyroid gland were preserved.

PITUITARY DISEASE: A CLINICAL STUDY OF THREE CASES.

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The main purpose of this paper is to record and comment upon several cases of pituitary disorder which present noteworthy clinical features. The literature of this complex subject has become so extensive that an attempt to epitomize it cannot be made here.

Much careful clinical observation and animal experimentation is still necessary to solve the hypophysis problem, especially in its interglandular correlations and in its role in the "sex-levelling" process.

Since Marie first directed attention in 1886 to this hidden gland as a factor in disease, it has been subjected to so much scrutiny that it is in danger of becoming overworked as a *causa morbi*. The association of destructive and atrophic lesions of the hypophysis with clinical manifestations is close. The dependence of dystrophia adiposogenitalis—typus Froehlich—on hypopituitarism may be considered as proved. This form, which is characterized by defective development of secondary sexual characteristics,

FIG. 1. A. B.—Sella measures 12 x 16 mm., Note thin retroposed and retroverted cantel. The skiagraph was taken from a normal male, aged forty-eight years, who suffered from migraine.

atrophic genitalia, hypotrichosis, and adiposity, has its prototype in animal experimentation. Cushing[1] says: "Our first experience, therefore, with hypophysectomized adult canines deprived of all but a fragment of the pars anterior disclosed a clinical syndrome with adiposy, increased sugar tolerance, lowered body temperature, and reversive sexual changes as its chief features. Later experiences, with the production of corresponding hypophysial defects in puppies, disclosed a similar syndrome, with a persistence of sexual

[1] The Pituitary Body and its Disorders, Philadelphia, 1912.

infantilism and the additional factors of skeletal undergrowth and evident psychical disorders."

The case is different in acromegaly. Although circumstantial evidence for a hyperpituitarism or perverted secretion of the pars anterior as its cause is most conclusive, yet it is not absolute. The operative experience of Hochenegg and Exner in acromegaly approaches the experimental in the definiteness of results.[2]

The case is much the same with gigantism, and as a working hypothesis, we must accept the dictum of Launois and Roy that gigantism is acromegaly in subjects whose epiphyseal cartilages are not ossified no matter what the age.

The sequence of hypophysial struma and disturbed sexual or skeletal development is not invariable. This is shown by one of our cases in which an eroded sella, 12 mm. x 16 mm. (Fig. 1), was found in a medium-sized man, aged forty-eight years. The only possible growth anomaly was delicately shaped hands and fingers. His sexual development and sexual life have been normal. The patient had long been a sufferer from proxysmal headaches, which were relieved after alkalization thoroughly carried out over a period of several years. Such cases must make us accept with reserve sellar deformity and enlargement, *i. e.*, hypophysial struma, as proof of dyspituitarism in seeking for an explanation of clinical facts.

The relationship of the pituitary gland to diabetes mellitus and insipidus will be taken up after the case reports.

Case I.—A. L., aged sixty-one years, came under observation in January, 1908. In August, 1907, after a hard day's work in a cold-storage room he suddenly became weak, dizzy, and faint; a hemoptysis of one pint of bright red blood followed. A second hemorrhage occurred the same evening after he had entered St. Joseph's Hospital. For three weeks he spat blood daily and was much troubled with weakness and drowsiness. An intermission of about two months was followed by another hemorrhage brought on by heavy lifting. He then reëntered the hospital, where he has since remained as an orderly.

During the winter of 1908 he had many attacks of the following description: After a couple of days of malaise, weakness, intense parietal headache, tinnitus aurium, vertigo, palpitation, and of periocular edema a sudden rise in temperature (102° to 104°), with hemoptysis, would occur. At such times an area 4 to 10 cm. in diameter of impaired resonance with fine moist rales could be demonstrated in the lungs. The area was always sharply localized and usually to be found posteriorly in the upper part of one of the

[2] Hochenegg, J., Operativ geheilte Akromegalie bei Hypophysentumor, Verhandl. d. Deutsch. Gesellsch. f. Chir., 1908, vol. xxxvii, pp. 80 to 85; Exner, A., Rückgang der akromegalischen Erscheinungen nach Operation eines Hypophysentumors, Wien. klin. Woch., 1909, vol. xxii, pp. 108 to 109.

lower lobes. With the onset of hemoptysis the edema of the eyelids would rapidly disappear. The hemoptysis and temperature would cease two or three days later. These attacks occurred at frequent intervals for four months, when only an evanescent edema of the eyelids reoccurred at intervals of decreasing frequency. The leukocytes during the attacks varied from 7100 to 9000. A conjunctival tuberculin test and repeated sputum examinations for tubercle bacilli were negative. Repeated physical examinations during the intermissions revealed nothing except a moderate pulmonary emphysema and rapidly enlarging finger tips, which were at first considered to be a osteopulmonary arthropathy. Six months later the marked changes which had taken place in his hands, feet, and face, the increase in weight, the kyphosis, etc., made the clinical diagnosis of acromegaly certain.

At present (January 14, 1914) the patient complains merely of occasional swelling of the eyelids and slight attacks of weakness and drowsiness, which pass quickly on lying down.

Status Præsens. The patient is a large, heavy-set, elderly man (since the onset of his trouble his weight has increased from 140 to 265 pounds), the countenance is conspicuous for its prognathism, prominent cheek bones, squareness, beetling shaggy eyebrows, thick lips, muddy, pasty complexion, and apathetic expression. There is distention of the supra-orbital veins, which becomes evident on exertion or excitement. The palpebral fissures are narrow, the fundi are normal, the teeth are poor, and the tongue is normal in size. The trunk, legs, and arms are massive, the hands and feet are spade-like, the phalanges are thick, heavy, and bulbous. There is a marked increase in subcutaneous fat, and the abdomen is pendulous. There is a well-defined kyphosis of the cervicodorsal spine. There is no adenopathy, no increased area of thymic dulness, and no pigmentation. The thyroid, tonsils, and testicles are small (his sexual potency has always been very low). Perimetric examination reveals contraction, especially of the temporal fields, and a moderate interlacing of the color fields. The sella measures 17 x 11 mm., (Fig. 2). The dorsum epiphii is retroposed and retroverted. The posterior clinoid processes are thickened. The sphenoparietal sinuses with their branches are especially marked. The dentations of the lamboid suture are large and the digital impression are rather better defined than usual.

The patient took 400 grams of levulose at one time without excreting sugar. The most interesting features in this case are the peculiar angioneurotic edema of the periocular structures and the striking pulmonary phenomena. The character of the sputa and the dulness suggested infarct. The absence of cause for infarction and of disturbed general pulmonary circulation pointed rather to either an ephemeral pneumonia or an evanescent, intense, localized hemorrhagic edema of the lungs. Pneumococci were

not found in the sputa in any numbers, and the clinical course, observed during repeated attacks, was not that of abortive pneumonia. The best explanation is that it was a process similar to and of the same etiology as the edema of the eyelids, which always preceded or accompanied the lung manifestations. The anatomical lesion must have consisted of *congestion of a sharply localized lung area, with extravasation of blood and serum into the alveoli* extensive enough to impair resonance. Whether the association of the above-described syndrome with hypophysis disease is of any significance must be determined by other observations.

His subnormal sexual life and development as suggestive of a veiled hypopituitarism persisting until his fifty-sixth year is also of interest.

FIG. 2, A. L.—Acromegalic. Sella measures 11 x 17 mm. Note the retroversion, the retroposition, and the thickening of the dorsum epiphii. The sella also appears "dished."

CASE II.—M. V., aged twenty years, consulted me April 4, 1909, for amenorrhea and for *transitory disturbances in her ability to express her thoughts in words*. There had been four such "spells" in the preceding three months. She had suffered an epileptiform attack the preceding day, followed by a dazed state and severe headache. The right arm was limp for a few moments. There was nothing of significance in the family or previous history.

Physical examination showed a large, fat girl with undeveloped breasts; there was no pubic or axillary hair; there was a slight

congenital asymmetry of the face; the eye muscles and fundi were normal; the power of the dorsal flexors of the right foot was diminished; the knee- and ankle-jerks were sharper on the right side, and there was a positive Babinski on the same side. There was no adiadokokinesis or Romberg's sign; the abdominal reflexes on the right side were diminished; the uterus was infantile. Otherwise the physical examination showed nothing of significance. A diagnosis of *intracranial neoplasm affecting the hypophysis—typus Froehlich*—was made.

July 30, 1910. The following notes were made: The patient has grown very rapidly during the past year. Nocturnal epilespy has been common. The face was large, the skin coarse, and the expression stupid. The hands and feet were large and long, and the jaw was undershot. There had been a slight development of the pubic hair. The right masseter seemed weaker than the left The examination of the nervous system revealed the same findings as formerly. The patient was put on pituitrin (P. D.) ℞x, t. i. d.

December 1, 1911. The menses have been practically normal since the pituitrin was started. The pubic and axillary hair have developed moderately. Headaches, vomiting, and attacks of unconsciousness have been less than formerly.

September 28, 1912. The following was noted: The patient has only missed two menstrual periods in the last two years. She has become much heavier and more obese. The features have grown coarser and cerebration very slow. She complained of frequent attacks in which she became dazed and everything seemed unreal—*uncinate attacks without olfactory aura.* The acromegalic features were marked. There was a considerable amount of spotted brown pigmentation all over the body, which had appeared since last seen (adrenal insufficiency). There was weakness and slight spasticity of the muscles of the right upper and lower extremities. The tendon reflexes on the right side were all increased; Babinski, Oppenheim, and Gordon reflexes were all present on this side. The abdominal reflexes on the right side were gone. The facial muscles were distinctly weaker on the right side; the fundi were normal; perimetric examination showed interlacing of the color fields and contractions of all of the fields, especially on the temporal side; 150 grams of levulose, 350 grams of levulose, and 400 grams of glucose were given on different days and the urine collected; there was no glycosuria.

The sella measures 13 x 15 mm. (Fig. 3). The triangular excavation into the sphenoidal cells is noteworthy. The digital impressions were specially well marked in this case. The unusual shape of the sella and the secretory phenomena would lead one to suspect an infiltrating growth arising from the hypophysis, although the focal symptoms would point rather to an *interpeduncular growth which interfered with the infundibulum and consequently*

with the cerebrospinal fluid. The osseous overgrowth associated *with increase* in carbohydrate tolerance is significant, inasmuch as diminution in carbohydrate tolerance has been frequently noted in hyperpituitarism.[3] The transition of a hypopituitarism of the Froehlich type into a hyperpituitarism resulting in acromegaly is striking—hyperactivity of the anterior lobe with deficiency of the posterior lobe—and demonstrates the clinical existence of disassociation of the anterior and posterior lobes.

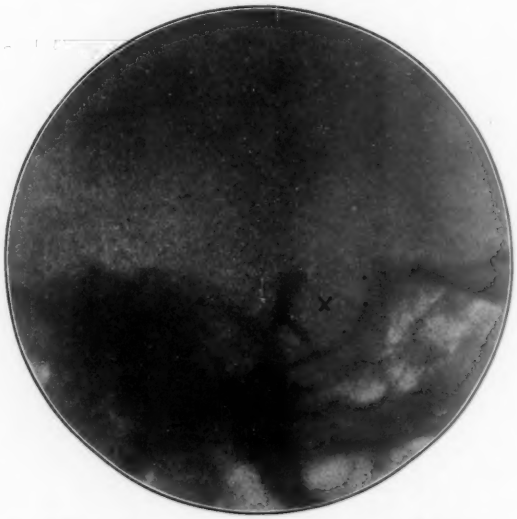

FIG. 3, M. V.—Sella measures 13 x 15 mm. Note the peculiar pyramidal shape which suggests erosion of the floor by an infiltrating process.

CASE III.—Mrs. N. was referred to me by Dr. Dierker, of Lawrence, September 1, 1913. She is twenty-three years old, has been married four years, has borne two healthy children, and has had no miscarriages. The family and past histories were negative. The present complaint began one year ago, four months after parturition. The onset was gradual, and the first thing noticed was that she was inclined to mope in a corner and show marked mental sluggishness.

The patient complained only of tiring easily and of attacks of dizziness, weakness, and depression, which come on suddenly. During the past year she has gained forty pounds, and a marked

[3] Cushing, loc. cit.; Ravault, Bull. et mém. Soc. méd. d. hôp. de Paris, 1900, vol. xvii, pp. 352 to 360; Borchardt, L., Funktion u. funtionelle Erkankungen der Hypophyse, Ergebnisse der innere Medizin u. Kinderheilkunde, 1910, vol. iii; Leri André, Akromegalie, innere Sekretion u. Nervensystem, Berlin, 1913, pp. 281 to 313.

change has taken place in her facial contour. There has been no gastro-intestinal, genito-urinary, or cardiovascular disturbances. She has suffered occasionally from occipital headaches.

The menses began at the age of fourteen years, and have always been normal. She married at the age of nineteen, and her husband states she was sexually undeveloped, and that there was no intercourse during the first year of marriage.

The patient was a large, dull, heavy-set, obese, apathetic young woman; she took little interest in her surroundings, and was unreasonable and inclined to be peevish and unruly; she would laugh or cry by the hour or sit as if in a trance. One day she spent two hours looking out of the window without changing position. Her face was square, the supra-orbital ridges were prominent, and the cheek bones protruded rather conspicuously; the face was flattened and heavy, but there was no special prognathism; the tongue was not thickened. The body was massive; the subcutaneous fat was abundant; there was a moderate growth of genital and axillary hair, with quite a little hair scattered along the linea alba. Examination of the heart, arteries, abdomen, and reflexes revealed nothing abnormal; there were no sensory disturbances; the urine was normal, although the daily output was only 400 to 600 c.c. Satisfactory perimetric observations could not be made.

The following tests to determine the carbohydrate tolerance were made: 150 grams of glucose were given in tea; on the second day 300 grams of glucose were given in tea; on the third day 450 grams were given in lemonade. After each administration the urine was collected for eight hours. In none of the tests was a reducing substance found. Marked diminution of urine was noted while these tests were in progress.

The sella measured 10 x 13 mm. (Fig. 4). There is some retroversion of the cantel, and the posterior clinoid processes seem thickened.

Fifteen minims of pituitrin (P. D.) were given hypodermically A.M. and P.M. This resulted in considerable loss of weight and a notable improvement in her mental condition.

The sexual history of the patient is important. The possibility of an antecedent hypopituitarism, manifested by complete absence of libido, with normal procreative functions, is of interest. Sexual intercourse was granted only at rare intervals, and then under protest. The lack of interest in husband, home, children, and in her wifely duties in general was significant. The husband believed her mentally unsound, and desired that she be committed; therefore the case assumes a medicolegal aspect. A report received February 4, 1914, states that she has lost about twenty pounds in weight and that she has become more active sexually. She has taken Armour's desiccated pituitary gland tablets in an irregular and desultory fashion.

The mental hebetude, lack of initiative, psychical depression, and negativism in this case strongly suggested the hebephrenic type of dementia precox. The increased sugar tolerance, osseous changes, physiognomy, and the clinical course spoke for pituitary disorder. It would seem well to bear in mind the possibility of pituitary disease in suspected cases of dementia precox corresponding to the above-described patient. Likewise the class of cases commonly designated as "fat anemics" should be analyzed with a possible pituitary disturbance in view. This condition commonly affects women about the menopause, and is characterized by increased fat, secondary anemia, and the whole train of neurotic

FIG. 4.—Sella measures 10 x 13 mm. The dorsum epiphii appears thickened. Acromegalic symptoms are developing rapidly in this case, although the sella is not markedly changed.

symptoms. The treatment of these cases is highly unsatisfactory, as they react little to the ordinary therapeutic measures. One of these women upon whom operations, rest cure, forced feeding, suggestion, corpus luteum, etc., had been tried, improved markedly on pituitrin. Her sella measured 10 x 13 mm., and her physiognomy strongly suggested acromegaly (this change developed markedly while under observation).

The scope of this paper does not permit of a systematic treatment of the symptomatology of pituitary disorder, and we wish merely to consider briefly the sellar phenomena and certain secretory disturbances.

The roentgenological skull findings in hypophysis disease are manifold and often difficult of interpretation. Sellar enlargement does not necessarily mean *clinical* hypophysis disease, nor does an extremely small sella mean hypopituitarism; therefore much care must be exercised in the interpretation of sellar changes.

The following types may be considered:

1. *Intrasellar growths* widen and deepen the sella so that its floor approaches the floor of the middle fossa. The dorsum epiphii is thinned out, shoved backward, tipped backward, and elongated. Often the posterior clinoid processes partake of the general osseous overgrowth in acromegalics. Changes elsewhere in the skull are often demonstrable—namely, prognathism, large sphenoidal, frontal, and superior maxillary sinuses, thickened skulls, widened sphenoparietal sinuses, digital impressions, and broad sutures with excessive suture indentations.

2. *Extrasellar growths* tend to produce dishing.[4] The cantel is widened, thinned, and shortened; the floor maintains its normal relation to the base of the skull; acromegalic changes, as a rule, are absent, and there is rather thinning than thickening of the skull.

3. *Large hypophysis tumors* may give rise to complete destruction of the sella, often invade the sphenoidal sinuses, and rarely they may completely destroy the body of the sphenoid. Their extra- or intrasellar origin often cannot be determined at this stage. The anterior clinoid processes may point to their origin, *i. e.*, they are often pushed upward and elongated in intrasellar growths while they are shortened in extrasellar growths.

4. Processes which give rise to increased intracranial pressure will frequently produce changes in the sella. They are more inclined to affect the sella asymmetrically; occasionally basal tumors will distort the sella in such manner that roentgenological differentiation is impossible. Tumors arising in the sphenoid itself may even destroy the surrounding structures and leave the sella more or less intact.[5]

The value of good plates in obscure disorders of growth and of sexual development and activity, and in symptoms pointing to intracranial mischief, can hardly be overestimated. Disturbances of vision, migraine, epileptic attacks, psychical anomalies, trophic disorders—such as obesity, infantilism, impotence, gigantism, dwarfism, menstrual disturbances, without pelvic explanation—should call for an *x*-ray examination. We have been able to watch the development of pituitary disorder in two epileptics in whom the plates showed sellar deformation. Cushing's case of migraine,

[4] Schüller, Artur, Roentgen-Diagnostik der Erkrankungen des Kopfes, Wien. u. Leipzig, 1912.

[5] Schüller, loc. cit.

which was completely relieved by sellar decompression, is worthy of note in this connection.

Recently much evidence has been brought forward to prove the association of diabetes insipidus with pituitary disease. Frank[6] goes so far as to maintain that all diabetes insipidus is due to posterior lobe hyperactivity. Hypophysectomized animals excrete several times the normal amount of urine in the days following operation.[7] The same fact has been observed in operated cases. Often glycosuria is present in the first days, to be followed later by an increased sugar tolerance.[8] This is in keeping with the fact that acromegalics often show decreased sugar tolerance during the developmental stage and later show increased tolerance. Goetsch, Cushing, and Jacobson found in their experiments on carbohydrate metabolism following partial hypophysectomy that there was a transient glycosuria followed by increased carbohydrate tolerance, which could be reduced below the normal by the administration of posterior lobe extracts. A remarkable case has recently been reported by Simmonds[9] in which a diabetes insipidus followed a carcinomatous metastasis into the pars posterior in which the normal structure was almost entirely destroyed. The pars intermedia and pars anterior were intact. In two cases of diabetes insipidus observed by us the sugar tolerance was high; 450 grams of glucose were given at one time without the appearance of sugar in the urine. The curious fact was observed that *while taking the large amount of sugar the quantity of urine was markedly diminished.* Sellar changes were present in three cases of diabetes insipidus studied, either as enlargement, deformation, or erosion.

The following nosological schema, although not comprehensive, will serve to sketch the conditions resulting from the failure of the pituitary gland to discharge its particular functions in the interlocking glandular directorate which controls metabolism, growth, and sexual life:

1. Affections of the pars anterior:
   - (*a*) Hyperfunction—acromegaly, gigantism.
   - (*b*) Hypofunction—true or pituitary dwarfism (not chondrodystrophic, rachitic, or cretinic dwarfs).
2. Affections of the pars posterior:
   - (*a*) Hyperfunction—diabetes insipidus.
   - (*b*) Hypofunction—hypophysial obesity (dystrophia adiposogenitalis).

[6] Ueber Beziehungen der Hypophyse Zum Diabetes Insipidus, Berl. klin. Woch., 1912, p. 392.

[7] Crowe, Cushing, Homans, Quart. Jour. Exper. Physiol., vol. ii, pp. 389 to 400.

[8] Goetsch, Cushing, and Jacobson, Carbohydrate Tolerance and the Posterior Lobe of the Hypophysis Cerebri, Bull. Johns Hopkins Hosp., 1911, vol. xxii, pp. 165 to 190.

[9] Münch. med. Woch., No. 60, pp. 127 and 128.

3. Mixed affections:
   (*a*) Hyperfunction of the pars anterior with hypofunction of of pars posterior—acromegaly with hypophysial obesity.
   (*b*) Hypofunction of both lobes—dwarfism with hypophysial obesity.

4. Hypophysial disturbance, in conjunction with perverted activity of other glands.
   (*A*) Ovarian or testicular hypofunction with:
      I. Hyperfunction of pars anterior—acromegaly with sexual impotence—eunuchoid giants.
      II. Hypofunction of the pars anterior—pituitary dwarfism with sexual impotency.
      III. Hypofunction of pars posterior—dystrophia adiposogenitalis—genital obesity.
   (*B*) Associated with disturbances in the functions of other ductless glands, *i. e.*, adrenals, pancreas, thyroid, pineal gland, thymus (status thymolymphaticus), etc.

MENTAL MANIFESTATIONS IN TUMORS OF THE BRAIN.

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A review of the literature concerning mental disturbances in cases of tumor of the brain shows that it is impossible in the light of present knowledge to determine with any degree of accuracy in what particular tumor a certain group of mental manifestations will occur, neither is it possible to draw definite inferences from the seat of the tumor. The literature on this subject is abundant. Classifications have been attempted and tables drawn up to show the frequency of mental disturbances in tumors of various localities of the cerebrum, but a close analysis reveals contradictory statements from equally competent authors.

Some writers believe that in the majority of cases of tumors of the brain disturbances of intellect are observed. They vary from simple intellectual sluggishness to global dementia. The following manifestations are most frequently observed. A stuporous state predominates in the majority of cases. Whether it is exclusively under the influence of the severe pain in the head or it is independent of the latter it is not always easy to interpret. A state of somnolence is quite usual. Indifference and apathy are common. The patient shows lack or loss of interest in surroundings. An intellectual

effort and initiative are frequently in abeyance. In fact, Dupré and Devaux[1] observed in some cases a certain childish mental attitude (puérilisme psychique). The patients are infantile in their replies, in the intonation of their voices, in the mimicry; they show impatience and obstinacy characteristic of children in their motives and desires. In contrast with apathy and indolence, not infrequently we meet with undue irritability, emotionality, abulia, outbrust of passion and anger. The mnemonic faculties are frequently affected and not rarely from the beginning. The patient cannot recall names and events, and may give the impression of commencing paretic dementia.

The mental disturbances just enumerated do not, as a rule, constitute an embarrassing element in diagnosis of brain tumors, as the other characteristic manifestations of the latter do not fail to make their appearance, such as severe headache, vomiting, vertigo, etc. The difficulty lies in discriminating those cases in which the mental symptoms alone are present for a long time before the physical phenomena develop. Oppenheim and Wallenberg[2] reported such cases. The diagnosis is also difficult in cases in which the characteristic symptoms of the classical psychoses are present or are predominating in the clinical picture. Melancholia, mania, dementia precox, acute hallucinatory delirium, paretic dementia, all have been diagnosed and postmortem revealed the presence of tumor in the cerebrum.

If we turn our attention to the localization of the tumor and attempt to draw inferences as to a certain relationship between these two factors, we again meet with failure. The presence of a tumor in any region of the brain cannot explain the accompanying psychic disturbances, and the latter cannot therefore be considered pathognomonic of the first. Otherwise speaking a diagnosis of tumor cannot be based on the presence of certain special mental manifestations. Some writers attempted to build clinical pictures special to the frontal lobes, to the corpus callosum, to the temporal lobes, and to other portions of the brain. Thus change of character, such as suspiciousness, hostility, violence, has been attributed to tumors of the frontal lobe. Jastrowitch describes under the name of "moria" and Oppenheim under the name of "Witzelsucht" a jovial and humoristic state of mind as characteristic of tumors of the frontal lobe. In diseases of the same region other writers observed various mental phenomena, such as enfeeblement of intellect, depression or childishness (Dupré). Symptoms of paretic dementia have also been observed in tumors of the frontal lobe.

On the other hand, similar identical psychic disorders have been seen also in tumors of the psychomotor zone and even in central tumors. Delusions, hallucinations of all varieties, confusional or

[1] Nouvelle Iconographie de la Salpêtrière, 1901.

[2] Specielle Pathologie und Therapie von Nothnagel, Band ix, Th. 1, Abth. 3.

delirious states characteristic of genuine psychosis, may all accompany tumors of the brain. Complete clinical pictures corresponding to the well-established forms of insanity have also been observed in the course of cerebral neoplasms. In one of my unpublished cases a man, aged thirty-five years, presented for months the alternating phases of manic-depressive psychosis. The maniacal periods were particularly long and pronounced. There was not a single somatic symptom indicative of intracranial pressure for a long time, and only three months before he died, papilloedema developed. Patient was operated on and a large tumor was found in the temporosphenoidal lobe of the left hemisphere. In one of my cases which I am about to report the clinical picture for many months was that of paretic dementia, and only shortly before death excruciating headache and vomiting made their appearance. The disease progressed rapidly. At autopsy a tumor was found in the basal ganglia of the left hemisphere.

Among extensive statistical studies of mental symptoms in cerebral tumors those of Shuster and Knapp deserve special mention. The first author in his *Psychische Störungen bei Hirntumoren* reports 775 cases. In 423 cases chiefly mental weakness and dementia were present. In the remaining 352 cases he observed gross mental disturbances suggestive of distinct classical psychoses. The most conspicuous among the latter presented maniacal states (95); the next in proportion were the depressive states (57); then the deliria with hallucinations (52); general paralysis 29 cases and paranoia 19 cases.

In Knapp's tables,[3] drawn from a smaller number of cases, we also find clinical pictures of paresis, of delirious, confused, and maniacal states, also of paranoia. Hallucinations are also mentioned. Shuster is apparently inclined to believe in a certain relationship between the type of mental disorder and the seat of the neoplasm, but a close analysis of his records as well as those of other competent observers does not justify any pathognomonic conclusions; neither can any definite relationship be established between the mental disturbances and the nature of the growth.

The pathogenesis of mental manifestations in the course of brain tumors is debatable. The tolerance of the brain for foreign bodies and growths is well known. There are many cases on record showing the presence of voluminous tumors in various areas of the brain without mental disturbances. Multiple tumors have been observed in the same brain without any mental disorder during life. Softening of vast areas in the brain have been observed also without morbid mental symptoms. These facts tend to prove that destruction of one limited area of the brain substance is not sufficient to produce psychic disturbances, that the intellectual

[3] Brain, 1906, vol. xxix.

faculties are dependent upon simultaneous coöperation of all constituent portions of the brain. However, mental disturbances have been observed in tumors affecting but limited parts of the brain. Explanations have been sought in various hypotheses. Generalized compression, generalized irritative action caused by localized tumor, auto-intoxication, are the views advanced by various authors for the existence of the mental symptoms. The doctrine of auto-intoxication finds its *raison d'être* in the assumption of continuous absorption of toxic elements originating in the tumor by the venous and lymphatic circulation. The analogy between the clinical picture of uremic encephalopathy and that of cerebral neoplasm is striking. The delirious, hallucinatory symptoms can be readily explained by the toxic pathogenesis. Klippel[4] believes that we have to deal here not only with an auto-intoxication but also with a secondary infectious process. The latter develops around the tumor and gives place to an inflammation. Not infrequently we find at autopsy an acute inflammation in the close vicinity of the tumor, in the meninges, in the ventricles. Thus headache, convulsions, delirium, fever, coma find their explanation.

Intracranial pressure, generalized irritation, auto-intoxication, and secondary infection may all render considerable assistance in attempts to explain the presence of a great many mental manifestations accompanying cerebral tumors. When, however, we wish to interpret the development of genuine psychoses in the course of brain tumors, the above views fail to give an adequate explanation.

One of the cases here reported presents the most striking resemblance with paretic dementia both from the stand-points of physical and mental manifestations; yet no meningo-encephalitis was found, and a tumor was seen in an area not at all suspected during life. Neither of the above views explains the clinical picture which for a long time remained almost typical of the great psychosis. Only during the last three months signs of intracranial pressure made their appearance. A negative Wassermann reaction both of the blood and cerebrospinal fluid was also one of the most unexpected occurrences, and rendered considerable assistance in making a diagnosis. The second case is one of a tumor of the pituitary body. During life the mental phenomena were of such a nature that the diagnosis of paresis was repeatedly made by competent men. The third case is one of a tumor situated between the frontal lobe and insula in the left hemisphere. During life the patient presented a very marked dulness, apathy, indolence, and extreme somnolence.

CASE I.—C. A. O., aged fifty-six years, contractor of iron works by occupation, drank beer heavily until the last four years of his

[4] Traité de Médecine de Brouardel and Gilbert, article Tumeurs cérébrales.

life. His family history is unimportant. While travelling in foreign lands twenty years ago he contracted yellow fever and erysipelas, from which he completely recovered. He denied venereal diseases.

Four years ago he developed epileptic seizures. They occurred at first occasionally, but they became quite frequent within the last year. Every week or two weeks he would have an attack, and exceptionally two in the same day. The patient's wife's statements as to the seat of the convulsions were not always the same. Sometimes she thought they were confined to the right side and at another time she would say that she observed them on the left side. Ten months before he died he developed hemiplegia on the right side. The paralysis was at first very slight, but it gradually progressed. Since the onset of the paralysis the wife noticed a gradually oncoming change in the patient's mentality. He became at first listless, inattentive, then he began to be careless about his habits. He would spit on the floor, would not change his underwear for two weeks at a time, would soil his clothes when in the toilet (prior to his present illness he was exceedingly particular about cleanliness and neatness). When reproached he would laugh and agree that he was wrong, but would soon forget it. His memory began to fail about a year ago. Mistakes were noticed in writing letters: he would omit letters and sentences. He began to forget names. He could not recollect voluntarily facts of importance, such as business transactions and money matters. On one occasion he received several checks, and a half-hour later they could not be found. They were recovered the next day in the vestibule of his house on the floor near the hall stand. Shortly afterward the wife noticed a difficulty of expressing himself: his speech became thick and certain letters could not be pronounced clearly.

When he presented himself for examination three months before he died I observed the following conditions: He was distinctly hemiplegic on the right side. His paralysis, however, was not pronounced. The leg was only slightly dragged when he walked. There was no marked rigidity in the arm and leg; nevertheless, the power of both was considerably diminished. The right knee-jerk was increased; there was no ankle-clonus; Babinski and paradoxical reflexes were present on the right. The biceps and triceps reflexes of the right arm were increased when compared with the left side. There was a slight deviation of the face to the right. The pupils were unequal: right larger than left; their contours were irregular. The right pupil reacted somewhat sluggishly to light; both reacted well to accommodation. A slight ptosis was observed on the right side. The right eyeball was somewhat protruded. An ophthalmoscopic examination showed a dilatation of the blood-vessels in both retinæ, but no profound changes in the papillæ. The state of the patient's mentality did not permit to determine whether there was diplopia or not. Ocular palsies were not present,

with the exception of a slight weakness of the left external rectus. The hands and tongue were affected with a fine tremor. There was some ataxia of the upper extremities. The stereognostic sense was preserved in the right hand, but he was unable to name all the objects placed in it. Asymbolia was therefore present for some objects. The general sensibility, objective and subjective, was affected on the right side. Touch, pain, and temperature were markedly diminished on the entire right side, face included. Besides, the patient frequently complained of severe pain in his right arm and leg. Considering the slightness of the motor paralysis, the case so far presented a thalamic symptom-group.

The sphincters were both involved. Involuntary micturition occurred quite frequently. Constipation was obstinate.

The patient's mentality suggested strongly paresis. His facies was drawn; his answers were slow and delayed; the speech was typically paretic, slow with special stoppage on letters *r* and *m*. He looked weak and exhausted, and at the same time he would say, "I feel fine; nothing ails me." He was unable to realize the paradoxical relation between his condition and answers. At times he would clear up and appear brighter, but this improvement would not last long. His memory was decidedly deficient. He was unable to recollect events of two or three days past. He would frequently call his wife by a different name. He could not tell what he ate two or three hours before. Dulness was very conspicuous. When interrogated, he would stare for a while before he would reply, and then the answers were sometimes without any relation to the questions asked.

The condition as just described, including the physical as well as the mental symptoms, suggested strongly the diagnosis of paretic dementia. Soon, however, the clinical picture commenced to change.

He began to complain of severe headache. Formerly he had headache only at the time of an epileptic seizure, but presently it occurred quite frequently and irrespective of attacks. The patient began to have vomiting spells. In the last month they occurred daily and independently of food. His mentality became more and more deeply affected. He had to be fed, he ceased to recognize distinctly his surroundings. The headache became intense, so that he could not sleep; he groaned continuously. The epileptic attacks became very frequent. The hemiplegia became deeper. The vomiting became almost continuous. Finally coma set in and the patient expired after several violent convulsive attacks rapidly succeeding each other.

While under my observation during the last three months of his life the patient was kept in bed with the exception of occasional brief intervals. Thus opportunity was given to study him from every stand-point. Except the liver, which was enlarged, the other

internal organs were found intact. The urine at first contained albumin, which later disappeared entirely. The blood examination as to its physical properties was normal. In view of the clinical evidences of paretic dementia a Wassermann test was made before any treatment was instituted, on the blood-serum and cerebrospinal fluid. To my great surprise the result was negative. A

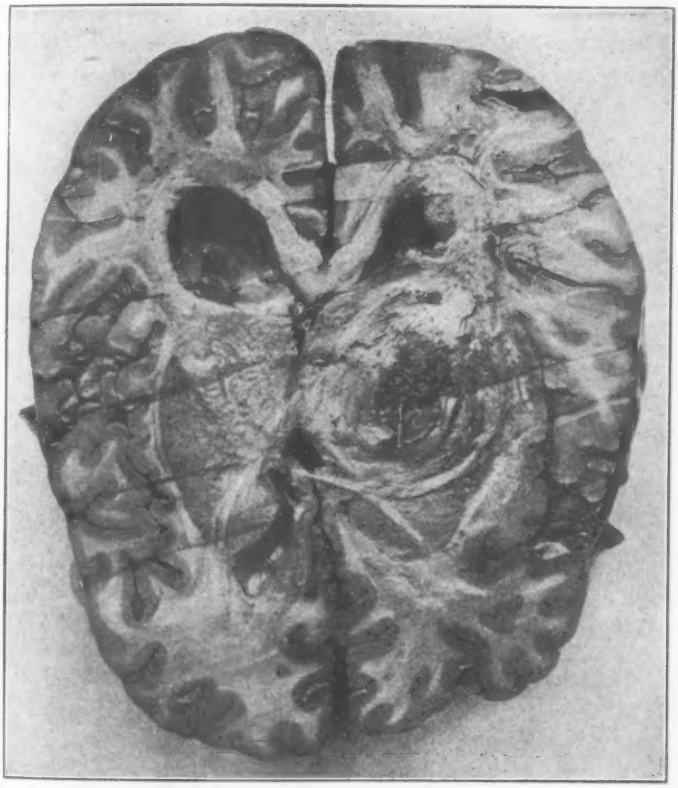

FIG. 1.—Mixed-cell sarcoma in the basal ganglia of left hemisphere.

month later the test was repeated, and again the reaction was negative. The cytological examination of the cerebrospinal fluid showed the presence of a number of lymphocytes and a few polynuclear cells. Each lumbar puncture showed a marked increase of pressure in the subarachnoid cavity, as the cerebrospinal fluid emerged with great force.

The negative Wassermann reaction, in spite of the distinct

clinical symptoms of paresis, made me reject the latter diagnosis. Subsequent events mentioned above proved the case to be one of cerebral neoplasm simulating paredic dementia.

Autopsy performed twenty-four hours after death revealed the following: The heart, lungs, and kidneys were apparently normal. The liver was enlarged and hard. The scalp and skull were of normal thickness, and presented no abnormalities. The dura was pale and the vessels were bloodless. A noticeable feature of the dura was its thickness and resistance to cutting. On the left side, in front of the anterior end of the longitudinal fissure, the brain protruded in spots through the dura. This area, of the size of about a square inch, resembled a leaf which was moth-eaten; the dura covering this area was extremely thin.

The brain was remarkably dry, and there was little fluid after its removal. A tumor was found at the base of the left hemisphere of about the size of an almond. It resembled a convolution which had been pushed out from above downward and from behind to the left of the pons (Fig. 1).

The cord was apparently normal. A transverse anteroposterior section of the brain revealed a large tumor within the basal ganglia of the left hemisphere, destroying the largest part of the caudate and lenticular nuclei, also the adjacent part of the optic thalamus, pushing backward, forward, and externally the neighboring tissues. The tumor extended downward to the base, where it appeared on the side of the pons covered by the cortical substance. Histologically the tumor presented a mixed-celled sarcoma. Below the tumor the tracts were in a state of degeneration.

Case II.—H. S., aged thirty-one years, a watchmaker, was apparently well until the age of twenty-three. At that time the following symptoms developed gradually: ptosis of the left upper eyelid; diplopia; diminution of visual acuity of the left eye; vertigo; headache. The mental phenomena consisted of frequent attacks of loss of consciousness followed by a confusional state lasting two to three weeks at the time. The patient also showed a fine intention tremor of the hands and of the tongue. This condition lasted five years, during which the diagnosis of paretic dementia was made by several competent men.

At that time he began to develop the following symptoms: Bitemporal hemianopsia, optic atrophy in the left eye and optic neuritis in the right eye. Further examination revealed strikingly infantile genitalia and lack of sexual desire. Soon a descending right hemiplegia made its appearance. The patient began to increase in weight; he became markedly adipose, so that six months before he died he weighed 235 pounds. He became enormous. The attacks of unconsciousness continued, and they were followed by prolonged confusional states as before. The adiposity, the bitemporal hemianopsia, with increasing blindness, the infantile genitalia—all

finally suggested an angiosarcoma of the pituitary body which was verified by autopsy (Fig. 2). For a long time the case presented the picture of paresis until the characteristic eye symptoms and the adiposity began to make their appearance.[5]

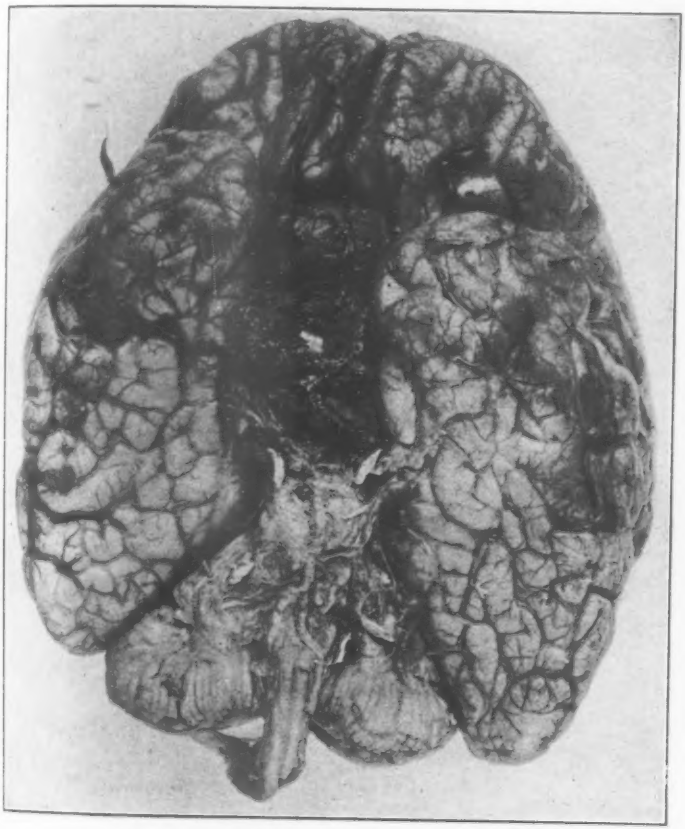

FIG. 2.—Tumor of pituitary body (angiosarcoma).

CASE III.—An Italian boy, aged sixteen years, presented for a long time headache, gradual loss of sight, ataxic gait, loss of knee-jerks, and Achilles tendon reflexes on both sides, with Babinski on one side and paradoxical sign on both sides. The eyes soon showed a high degree of papillitis. The patient's speech was slow. Mentally he presented a marked dulness, apathy, and indifference

[5] Jour. Amer. Med. Assoc., 1912, lix, 171.

to surroundings. An operation failed to relieve him (Fig. 3). At autopsy a large round-celled sarcoma was found wedged in between the frontal lobe and the insula of the left hemisphere.[6]

FIG. 3.—Tumor (round-cell sarcoma) wedged in between the left frontal and temporal lobes, penetrating the lateral ventricle.

While the frontal lobe of the left hemisphere suffered considerable compression, nevertheless the mental manifestations consisted only of mental dulness and indifference. We have seen above the tendency of some writers to lay especial stress on the frontal lobe and to find especially grave symptoms which could be considered as pathognomonic of an involvement of this particular portion of the brain. This case speaks emphatically against such a view.

[6] New York Med. Jour., January, 1913.

PERIPHERAL PIGMENTATION OF THE CORNEÆ, ASSOCIATED WITH SYMPTOMS SIMULATING MULTIPLE SCLEROSIS.

By T. B. Holloway, M.D.,

PHILADELPHIA.

In 1902 Kayser referred to a peripheral annular pigmentation of each cornea in a patient whose nervous symptoms seemed to warrant a diagnosis of multiple sclerosis, and in the further course of the disease diabetes and pigmentation of the skin developed. Since the first report by Kayser, the histories of several other cases showing analogous ocular and nervous manifestations have been recorded. Recently the condition has been especially studied and discussed by Fleischer.

The clinical findings in the patient whose history is recorded below warrants the inclusion of this case in this particular group.

Mc G., aged twenty-seven years, was admitted to the University Hospital on the service of Drs. Charles K. Mills and William G. Spiller, December 12, 1912,[1] complaining of loss of control of his arms and voice.

History of Present Condition. The patient stated that he was perfectly well until the latter part of March, 1910, at which time he noted that the right hand would tremble and shake when he attempted to write. When writing it was necessary for him to steady the right hand with the left, and in a few months he was compelled to give up this method and do his writing with his left hand. In July, 1911, his voice became somewhat affected, so that he talked, as he expressed it, as "one who is afraid to speak." On December 25, 1911, he first became aware that the left hand was becoming affected in the same manner as the right. From that time on the tremor increased in extent and severity, until at the present time he is not able to button his clothes, brush his hair, or feed himself. This tremor disappears when he is quiet or after he has been in bed for a few minutes. In the summer of 1912 he first noticed that his head would start to shake, especially when he would talk. This also has increased in the past few months. For the past year there has been a jumping sensation in the muscles of his legs, as if they were contracting suddenly, but he has felt no loss of power, pain, or loss of control. This only occurs when he is lying in bed or sitting still, never when walking. Otherwise

[1] This patient was first seen by me late in the summer of 1912, through the courtesy of Dr. A. C. Sautter. He was then under treatment at the German Hospital, and had been referred to the service of Dr. W. T. Shoemaker, for ocular examination, where he came under the observation of Dr. Sautter. He was exhibited at the April, 1913, meeting of the Philadelphia Neurological Society.

the patient feels perfectly well; he has not lost in weight; sleeps well; in fact, is rather drowsy all the time. He never has headache, but has some dizziness when rising from bed or from a stooping position. His appetite is good; his bowels, as a rule, are regular, but for the last month he has been somewhat constipated. There are no cardiac or respiratory symptoms.

Previous Medical History. He has had the usual diseases of childhood. Since a boy he has been subject to vague rheumatic pains in the left arm and leg. No other sickness except gonorrhea a number of years go, which persisted for one year. He denies syphilis. He never sustained any injuries and never had any traumatic or inflammatory ocular condition.

Social History. He has been a painter for the last fourteen years, but has seldom used white lead, and none in recent years, his work calling for varnish. Mostly all of his work has been done in the open. He has used tobacco to excess. Since the summer of 1912 he has drunk very little, but prior to that he averaged seven or eight glasses of beer a day.

Family History. Negative. No history of nervous, cardiac, renal, or lung trouble.

Physical Examination. The patient is a large-framed individual, with good musculature; well nourished; no stigmas of hereditary lues. The face presents a distinctly dusky appearance, but the scalp is not affected. There is a suggestion of a fine capillarity over the cheeks and nose. On both legs over the anterior and outer surfaces there are large areas of brownish-yellow pigmentation, occurring in blotches. He thinks this has been present for about ten years. There are no evidences of edema. The skin is soft and moist. The peripheral arteries are not sclerosed. The pulse is slow and full and of fair tension.

Nervous System. The gait is normal. Station is good. There is a questionable tendency to Romberg's sign. The patellar, biceps, and triceps reflexes are somewhat exaggerated, but equal on the two sides. No ankle clonus; no Babinski sign. No change in the abdominal or cremasteric reflexes. There is no disturbance of sensation; the muscular power of the arms and legs is good. The tongue when protruded is not deviated to either side, but is accompanied by a slight tremor. The seventh nerve is intact. Speech is rather syllabic, slow, and deliberate. Heel-to-toe test is negative. Finger-to-nose test shows marked intention tremor. There is no propulsion or retropulsion. No dysphagia.

General System. The ears are apparently normal; the throat is negative; the teeth are poor; there is no blue line. The lungs, heart, liver, spleen, and abdomen are negative.

Ocular Examination. There is no true nystagmus, but at the extreme limits of the lateral rotations a faint nystagmoid jerk can be noted. The ocular rotations are not impaired. The pupils

are larger than the average, but react promptly and normally to the various reflexes. By oblique illumination an annular pigmented zone can be noted about the periphery of the cornea of each eye, which produces a distinct contrast in color between the covered and exposed portions of the blue iris. With a Zeiss loupe there can be noted an annular pigmentation of the cornea which apparently involves the deepest layers. In the right eye this pigmented area is widest above and to the nasal side, and narrowest below and to the temporal side. The width of the involved area varies from 2 to $3\frac{1}{2}$ mm. At the more peripheral portions it presents a smoky or brownish appearance, which fades into a brownish-green as the pigment disappears in the more central uninvolved portions of the cornea. The apparently clear central portion of the cornea is oval. With a Nernst lamp and a Zeiss corneal microscope there is a suggestion of a finely granular appearance toward the limbus, but this is not pronounced. The cornea is not vascularized, nor does it show any opacities that might be the result of congenital or inflammatory conditions. No pathological changes could be seen in the iris. With the opthalmoscope no opacities were seen in the lens or vitreous. The disks were nearly round, suggestive of a reddish-gray type, but no pallor of the temporal sector was seen; no evidences of neuritis. There were no vascular changes, and the choroid and retina were healthy. The fields for form and colors were normal, and no scotoma could be elicited either by the ordinary perimetric examination or by Bjerrum's method.

O. D. = .50 pp. 13.5 cm., with + .25 cyl. ax. 180 = $\frac{6}{5}$ +.

O. S. = .50 pp. 13.5 cm., with + .25 cyl. ax. 165 = $\frac{6}{5}$ +.

Progress of the Case.—December 16, 1912. Urine: cloudy and straw colored; sp. gr., 1011; alkaline; faint trace of albumin; sugar negative; bile, urobilin, and indican negative; casts, mucus, and red-blood corpuscles negative; occasional white corpuscles; amorphous phosphates and urates.

Blood. Red corpuscles, 4,330,000; white corpuscles, 7100; hemoglobin, 75 per cent.; polynuclear, 65; lymphocytes, 28; transitional, 2; eosinophiles, 5.

Blood Pressure. Systolic, 125; diastolic, 80.

Levulose Test. December 19: 65 grams of levulose in 200 c.c. of water were given on a fasting stomach and the urine collected every hour for five hours. Except for the third-hour test, which was spoiled, a positive reaction was obtained for each examination. (Dr. F. G. Sproul.)

Wassermann Test. Negative.

December 21. Examination by Dr. O. H. P. Pepper confirmed the above findings, but owing to several punctate bluish granules at the gum margin an examination for degeneration of the red cells was suggested. A slight cervical adenopathy was noted.

Feces. Light brown, semisolid; no fat or mucus; occult blood negative; slight trace of bile; plant cells, muscle fibres, epithelium, leukocytes, bacteria, yeasts, crystals, and debris.

Blood examination for basic degeneration was negative.

December 23. Stomach contents: specimen a creamy, turbid fluid, with granular sediment and brown specks. Free HCl, 60 per cent. (dimethylamidobenzol); total acid, 75 per cent.; lactic acid, 0; occult blood, negative; starch, yeast, bacteria, leukocytes, Oppler-Boas were negative.

February 6, 1913. Levulose test by Dr. J. Gordon Saxon: With 40 grams of levulose a typical reaction to resorcin was obtained for six hours; this was confirmed by spectroscopic examination. With 30 grams of levulose there was a similar result.

March 16. A test for increased sympathetic tonus was made by Dr. Arthur Hopkins and gave a positive result. A hypodermic ingection of ten minims of adrenalin (1 to 1000) was given and the case observed during the following hours. The blood-pressure was raised 18 points; marked tremor provoked; sugar tolerance markedly reduced and lymphocytes increase by 13 per cent.

A Röntgenogram of the head by Dr. H. K. Pancoast was negative.

May 4. Hemoglobin, 70 per cent.; red-blood cells, 4,050,000; white-blood cells, 7000.

During the several months the patient was under observation there was an improvement in his tremor, but aside from this there was practically no change. The station and gait remained normal, and no psychic phenomena developed. Drs. Hartzell and Knowles, who examined the skin lesions, reported a colloid degeneration of the skin of the forehead and a mild type of acne rosacea associated with a pigmentation of the legs, due to blood pigment, which occasionally follows erythematous eczema.

In 1910,[2] in an article on corneal pigmentation, I had occasion to causually refer to this particular type of pigmentation, but at that time I had never observed a case, and had overlooked a contribution to this subject by Fleischer in 1909.[3] This observer has especially studied the few cases of this character that have been observed or at least recorded, and has had opportunities to study the two cases that have come to autopsy, so frequent references will be made to his findings. Since I could find references to but five cases that exhibited this type of corneal pigmentation it may be well to review these histories.

In 1902 Kayser[4] reported from the Tübingen Clinic the history of a male, aged twenty-eight years, who for five years had what was regarded as multiple sclerosis. While the patient was not regarded as a confirmed alcoholic, the first symptoms developed after alcoholic excesses. In each eye there existed an annular

[2] Annals Ophthal., 1910, xix, 685.

[3] Münch. med. Woch., 1909, p. 1121.

[4] Klin. Monatsbl. f. Augenheilk., 1902, xl, ii, 22.

peripheral pigmentation of the cornea, which began at the limbus and gradually faded away centrally, so that a central oval area of the cornea remained normal. The widest part of the pigmentation was above and below, more in the former position. Examination with the Zeiss microscope did not reveal any abnormalities at the limbus or in the cornea itself, other than the pigmentation, which was dense enough to obscure the iris. The peripheral portion was noted to be made up of an accumulation of yellowish granules, which became finer and more diffuse centrally where the color changed to yellowish-green. This pigmentation was observed to be deep; the superficial and middle layers of the cornea were not affected. Fleischer had further opportunities to study this patient, and has reported on the later findings.[5] The patient was intermittently under observation up to the time of his death in May, 1909. During this period the nervous phenomena became worse, distinct psychic phenomena occurred, while late in the course of the disease there developed diabetes and a grayish-brown pigmentation of the head and hands, with grayish discoloration over the chest and abdomen. The liver was palpable, but not the spleen. There was no reduction in the visual acuity, but the pigmentation of the cornea increased, and there was some lessening of the light sense.

Autopsy. The liver was rather small and nodular, the spleen enlarged, and the kidneys pigmented. There was a small localized patch of thickened pia near the vertex. Macroscopically and microscopically there were no signs of multiple sclerosis. Microscopically the cornea showed a pigmentation of Descemet's membrane that extended centrally about 1.9 mm. The deposit consisted of rounded and angular greenish-brown granules that appeared refractile at a certain angle. This deposit was separated by a clear space from the endothelial cells, which were normal in appearance. The only other structure of the eye that presented any pigmentation was the hyaline membrane of the choroid or the membrane of Bruch. Here the deposit was more marked than in Descemet's membrane, and the granules finer than in the adjacent pigment epithelium and the pigment cells of the choroid. The interstices and fibres of the eye muscles were pigmented, as was the optic sheath, but the nerve itself was free. In the kidneys the basement membrane of the urinary tubules were especially pigmented. In the liver the pigment was found in the interacinal connective tissue. There were evidences of degeneration of the liver cells and proliferation of the connective tissue. The spleen was markedly pigmented, especially in the trabeculæ and walls of the bloodvessels, and also in the pulp, but here it was mostly extracellular. In the intestines the pigment was present in the

[5] Bericht der Ophthalmologischen Gesellschaft, Heidelberg, 1908, p. 128.

vessel walls and in the circular muscle. The connective tissue of the heart was pigmented, while in the skin the basal layer of epithelium was affected, also the connective tissue of the hair follicles and the basement membrane of the sweat glands. The pia was pigmented, but the lungs were free. The adrenals were normal. The condition of the pancreas was not described.

In the following year Fleischer[6] at the same clinic observed two similar cases. This first patient was a male, aged twenty-nine years, with a kyphosis. Venereal disease was denied and there was no history of alcoholism. The patient had a high hyperopia, congenital amblyopia, and horizontal nystagmus. Nervous symptoms in the form of an intention tremor first appeared a year before. This patient had the same type corneal pigmentation as above described. His neurological condition was regarded as pseudosclerosis. The patient later developed distinct psychic changes and an intermittent glycosuria. He died in February, 1906.

Autopsy. The consistency of the liver was increased, its surface nodular, and on section, increase of the connective tissue was noted. There were evidences of slight chronic emphysema and bronchitis. The cardiac muscle showed some degeneration, the left ventricle was hypertrophied and the aorta and coronary arteries were atheromatous. The spleen was enlarged. In the stomach there was a copious hemorrhage and the scar of a cicatrized ulcer. In the brain the lateral ventricles were dilated, there were evidences of a chronic external pachymeningitis and chronic leptomeningitis, but discolored sclerotic patches or focal brain lesions were not found. No mention was made of the condition of the adrenals or pancreas, and no microscopic examination was made.

The second case was a male, aged thirty-one years. The left eye had been enucleated, owing to severe corneal ulceration secondary to dacryocystitis, but unfortunately no microscopic examination had been made. The right eye presented the type of corneal pigmentation now under discussion. Nervous symptoms had existed for two or three years, and were attributed to multiple sclerosis.

The fourth case was observed by Salus.[7] The patient was a male, aged thirty-two years, who had been affected with nervous symptoms for a number of years. When seen in February, 1908, there was noted an annular brownish-green pigmentation of the corneæ, which presented a granular apearance when studied with the Zeiss microscope. The neurological condition was regarded as multiple sclerosis.

At the conclusion of Fleischer's[8] most recent article he has briefly referred to a fifth case that has been observed by Gallus.

[6] Klin. Monatsbl. f. Augenheilk., 1903, xli, p. 489.
[7] Medizinische Klinik, 1908, iv, 495.
[8] Deutsch. Zeitsch. f. Nervenheilk., 1912, xliv, 179.

as well as Westphal.[9] This patient was a girl, aged nineteen years, who had greenish discoloration of the corneæ and a tremor resembling that seen in pseudosclerosis, but up to the time of his report no discoloration of the skin or diabetes had developed.

Among the patients so far affected all have been young adults, and five of the six patients were males. Several of the case histories make reference to preceding rheumatic affections or pains in the extremities and in one case there existed prolonged gastric disturbance some time prior to the onset of the disease. In Kayser's case the symptoms first developed after alcoholic excesses; Salus' patient attributed his to exposure to cold. No probable cause could be found for the other cases. The fact that the patient whose history is above recorded was a painter seems to be significant, but he used lead but little in his work, and not at all for the past few years; there was no history of colic and no basic degeneration of the red cells. He was, however, a consistent beer-drinker, and in the use of varnishes would be exposed to methyl alcohol; however, there is no history or ocular indications of any acute intoxication from this latter substance, but the possibility of some influence brought about by the frequent use and handling of this substance cannot, of course, be denied. The most conspicuous symptom and the one that has been constant in all the cases has been the marked coarse intention tremor affecting the arms and head in all cases, and in some the lower extremities as well. In Fleischer's first case and in the one here recorded the gait was normal, but in the others it became rather spastic. In all of the cases the cranial nerves were normal. Fleischer in speaking of Kayser's case states that the speech was not scanning in type, but owing to the tremor it was difficult; in the patient whose history is here recorded the speech was certainly affected more than could be accounted for by the tremor alone, and further no change was noted when the patient was quiet. Kayser's and Fleischer's first patient were the only ones to develop psychic phenomena, and in each instance this change was pronounced. The knee-jerks were exaggerated in Kayser's and Fleischer's second case, as well as in the case above mentioned, but in Fleischer's first case they were normal. In Salus' case they were absent. Ankle clonus was intermittently present in Kayser's case; Salus does not refer to it; while in the other cases it was absent. The abdominal and cremasteric reflexes were absent in Salus' case and were affected late in Kayser's case; in the other cases no change was observed. Salus does not refer to Babinski's sign, but in the other cases it was absent. In Kayser's case the head and hands presented a grayish-brown pigmentation of the skin, while there was some grayish discoloration over the

[9] Since forwarding this manuscript to the editor, I have found reference to a recent article by Westphal (Archiv f. Psychiatrie und Nervenkrankheiten, 1913, li, Heft 1), but at the present writing the original is not available.

chest and abdomen. While I did not find any reference to skin pigmentation in the history of Salus' case, Fleischer states a brownish pigmentation of the head was observed. The condition of the face and legs in the case here recorded has been referred to above. Glycosuria has been observed twice, and in a third case, while there was no glycosuria, there did exist a decided reduction in the sugar tolerance.

All of these cases showed the same type of cornea pigmentation. A deep annular pigmentation beginning at the limbus, appearing brownish green in color, and in its denser peripheral portion presenting a "smoky" appearance. It can readily be overlooked, and in brown irides would be especially difficult to detect, even by a trained observer. It is also well masked by a mydriatic, owing to the retraction of the iris behind the pigmented area. Its true character can only be detected with a loupe. Aside from the pigmentation it can be said that in all cases the eyes were negative, and did not show the changes so frequently present in cases of true multiple sclerosis. The vision remained unaffected.

In the two cases that have come to autopsy there existed a cirrhosis of the liver, associated with splenic enlargement and other changes already alluded to.

REMARKS. The diverse and complex character of the symptoms exhibited by the patients who have shown this type of corneal pigmentation makes the study of this group of cases most interesting. Kayser at the time of his report regarded the pigmentation of the cornea as congenital. Fleischer in the following year, while he called attention to the association of the corneal condition with symptoms of multiple sclerosis, was doubtful of their direct connection, although he did not exclude the possibilities of the pigmentation being an acquired condition. In a later brief reference[10] to it he stated that he believed it to be in some way connected with the debilitated condition of the patients. Salus believed the neurological condition to be multiple sclerosis, and suggested that Fleischer's case, regarded as pseudosclerosis, was also one of multiple sclerosis, and he believed there was an undoubted connection between the corneal pigmentation and the nervous symptoms. He called attention to the fact that the pigmentation most closely resembled blood-staining of the cornea, and based his suggestion on the work of Lapinski in reference to degeneration of the vessels in lesions of the sympathetic, he thought it possible that owing to innervation disturbances in the canal of Schlemm there resulted a slow filtration from this canal and imbibition of the coloring matter of the blood by the deeper layers of the cornea. While the incomplete autopsy on Fleischer's case in 1906 gave some suggestion of the complex character of some or possibly all of these

[10] Klin. Monatsbl. f. Augenheilk., 1908, xlvi, 91.

cases, it was not until opportunities were offered for more careful study in the case first observed by Kayser that a pigmentation of the internal organs was definitely demonstrated. Fleischer has made a most painstaking study of this case, and in his recent able contribution has discussed the various phases of the conditions presented.

Since in both of the cases that came to autopsy there had existed a glycosuria, with the postmortem findings of cirrhosis of the liver and enlarged spleen, associated with marked widespread pigmentation of the internal organs in the one case, and in the other (Fleischer's) the macroscopic examination intimate the possibility of analogous pigmentation, the possibility of a hemochromatosis or bronzed diabetes was immediately suggested.

The pathogenesis of hemochromatosis is still obscure. Probably the most prevailing opinion is that the pigmentation is the primary condition; Letulle[11] has regarded the diabetes as the original factor, while Potter and Milne[12] state that "it would seem as if today we are warranted in stating only that cirrhosis of the liver is the primary condition; that the hemochromatosis, always in slight degree in liver cirrhosis, is in some cases very excessive, and causes a general pigmentation which eventually also involves the skin; and finally, that the whole process is not any definite symptom-complex, but a chain of circumstances which rarely seems to be completed." On the other hand, Sprunt,[13] supporting the opinion of Opie,[14] regards it as a distinct morbid entity, and states there is no evidence of any abnormal blood destruction. He considers it a metabolic disease, "manifested, especially, by a change in the chromogenic groups of the proteid molecule with the deposition of pigments, and believes that the fibrosis of the various organs is dependent upon pigmentary degeneration and the accumulation of pigment in the interstitial tissue.

In the case so thoroughly studied by Fleischer, instead of finding the iron-containing hemosiderin and the iron-free hemofuscin, which characterize cases of hemochromatosis, he found a pigment that did not give the usual reactions of these pigments, and its exact character has not been definitely determined, although he believes the pigment to be a blood derivative. For the exact chemical properties of the pigment found, the reader is referred to Fleischer's recent article. Owing to the conflicting reports concerning the character of the pigment present in this case, its careful study has added but little if any to our meager knowledge concerning the physiological and pathological body pigmentations.

While this group of cases has certain symptoms in common with those found in hemochromatosis, reference to some of the more

[11] Cited by Potter and Milne.
[12] AMER. JOUR. MED. SCI., January, 1912.
[13] Archives of Internal Medicine, 1911, viii. p. 75.
[14] Trans. Assoc. Amer. Phys., 1899, xiv. 253.

convenient articles bearing on the latter subject, such as those contributed by Opie, Blumer,[15] Potter and Milne, and Sprunt, failed to reveal any reference to cases associated with nervous phenomena such as characterized these cases, and no reference is made to any corneal pigmentation that has been observed; on the other hand, Fleischer shows that the ocular microscopic findings are quite different.

This same observer also considered the possibility of poisoning by various metals especially silver, and pointed out certain resemblances to cases of manganese poisoning. As to the latter substance, this can be definitely excluded in the case here recorded, by the history, and I dare say the same is true about the other cases in this group. Casamajor[16] has recently referred to 9 cases of possible manganese poisoning, and has reviewed the literature. In the one case of his series that came to autopsy a superficial inspection of the brain-stem blocks before embedding, suggested the possibility of slight changes about the lenticular nucleus.

As to silver, while a chemical examination of small pieces of the kidney and spleen in Fleischer's case seemed to show the presence of this metal, certain other tests seemed to make this improbable, and it was further pointed out that there was no history of the patient having taken silver; that in argyrosis no such nervous and psychic symptoms develop, nor is the pia pigmented. It was also stated that the cornea is never involved in argyrosis. While this may be the case after argyrosis produced by the ingestion of silver, Knies[17] has referred to a brownish pigmentation of the cornea after cauterizations with silver nitrate stick. In this case the corneal epithelium and endothelium were not involved, but the stroma, Bowman's membrane and Descemet's membrane, were pigmented, as were the large deep lymph spaces and the four straight eye muscles.

In the case studied by Fleischer, the pigment, so far as the eye was concerned, seemed to have a selective action affecting two of the three important hyaline membranes of the eye, the membranes of Bruch and Descemet, both of which contain elastic fibres. The exemption of the lens capsule was explained by him as due to difference in chemical properties.

Fleischer has also considered pseudosclerosis and diffuse cerebral sclerosis. Oppenheim[18] and Potts and Spiller[19] refer to the difficulties attending the diagnosis of pseudosclerosis, while Wilson is still more emphatic and thinks the term should be abandoned.

Volsch[20] has placed on record the history of a case that he believed

[15] Yale Med. Jour., 1912, xviii, 190.

[16] Jour. Amer. Med. Assoc., 1913, lx, 647.

[17] Klin. Monatsbl. f. Augenheilk., 1880, xviii, 165 (cited by Parsons, The Pathology of the Eye) Jahresbericht f. Ophthal., 1880, 194.

[18] Text-book of Nervous Diseases, translated by Alexander Bruce.

[19] Jour. Amer. Med. Assoc., 1905, xlv, 1455.

[20] Deutsch. Zeitsch. f. Nervenheilk., 1911, xlii, 347.

to be analogous to Fleischer's, and has seen fit to group these with certain other cases attributed to pseudosclerosis. In his case there was also a cirrhosis of the liver, but no pigmentation of the cornea or internal organs. While corneal pigmentation was not especially sought for, he thinks it unlikely that this could have been overlooked. Wilson,[21] in an admirable monograph, has recently called attention to a definite syndrome occurring in the course of progressive lenticular degeneration, which he describes as "a disease which occurs in young people, which is often familial, but not congenital or hereditary; it is essentially and chiefly a disease of the extrapyramidal motor system, and is characterized by involuntary movements, usually of the nature of tremor, dysarthria, dysphagia, muscular weakness, spasticity, and contractures with progressive emaciation; with these may be associated emotionalism and certain symptoms of a mental nature. It is progressive and, after a longer or shorter period, fatal. Pathologically it is characterized predominantly by bilateral degeneration of the lenticular nucleus, and in addition cirrhosis of the liver is constantly found, the latter morbid condition rarely if ever giving rise to symptoms during the life of the patient." In the four personal observations of the author careful ocular examinations were evidently made, in the other case histories reviewed by him, eight in all, the ocular reports were incomplete or wanting, but in no case was there any reference to a pigmentation of the cornea, and the eyes were normal in other respects as well. All of the cases that came to autopsy had a marked cirrhosis of the liver, but nowhere in his careful and elaborate reports does he refer to any pigmentation of the internal organs. Wilson thinks that in connection with the hepatic cirrhosis, which does not produce any clinical signs during the life of the patient, a toxin is probably generated which exerts a selective action on the cells and fibres of the lenticular nucleus. In the addendum he alludes to Volsch's case, and believes it belongs in the group of cases he has so carefully described. He also refers to Fleischer's case, but makes no positive statement in regard to it, although the inference is that he would similarly classify it.

In the patient whose history is here reported the essential signs and symptoms have been the tremor, the character of the speech, and the corneal pigmentation. While no glycosuria manifested itself, there existed a marked reduction in the sugar tolerance. As above noted, the skin lesion of the face was attributed to acne rosacea, while the yellowish-brown pigmentation of the legs was said to be due to blood pigment such as at times follows erythematous eczema.

It is at least interesting to note the marked positive reaction this patient gave to the test for increased sympathetic tonus, the

[21] Brain, 1912, xxxiv, 295.

tremor being most markedly exaggerated for a period of two days. In this country Barker[22] and Hopkins[23] have referred in detail to the vagotonic and sympathicotonic states, and I am much indebted to the latter observer for his interest in the present case. While our present knowledge of the so-called autonomic and sympathetic systems may not warrant our drawing any definite conclusion, the results are none the less interesting, especially in cases of this character where the pathogenesis is obscure and unknown.

With the uncertain results in the chemical and microchemical tests in the case studied by Fleischer, considering the opinion expressed by Wilson, and the absence of pigmentation in the cases studied by him, as well as in the case referred to by Volsch, one may well ask whether we are really dealing with an acquired pigmentation of the cornea that has any connection with the other symptoms noted in these cases?

Concerning this it may be pointed out that in the 6 cases that have shown corneal changes the pigmentation has been bilateral; the cornea and the intra-ocular structures have been free from evidences of any traumatic or inflammatory condition apt to be associated with corneal pigmentation. But excluding a high refractive error and squint that were present in one case, other defects or anomalies that might be regarded as congenital have been wanting, unless, despite two autopsy reports, we regard the neurological symptoms as dependent upon a true multiple sclerosis, and accept the views of Strümpell, Ziegler, and Müller[24] that this affection is due to a congenital tendency to proliferation of the glial tissue. While all of the cases except one (Salus) exhibited this type of pigmentation when they first came under observation, all of them had been otherwise affected for a year or more. None of these cases had conical cornea, and, at any rate, there is practically no resemblance between this and the superficial annular pigmentation described by Fleischer and Hudson[25] as having been observed in cases of keratoconus. In one case (Kayser's) the pigmentation was said to have increased while the patient was under observation. To the best of my knowledge corneal changes of this character have not been observed or at least recorded except in association with the symptoms noted in these patients. Even if one accepts the report of the presence of silver (kidney and spleen) in Fleischer's case and eleminates the possibility of an associated pigment, it is hardly reasonable to suppose that all six of these cases had argyrosis.

[22] Trans. Assoc. Amer. Phys., 1912.

[23] Preliminary report read before the Section of Medicine, College of Physicians of Philadelphia, February, 1913.

[24] Cited by Oppenheim, Text-book of Nervous Diseases, translation by Alexander Bruce, vol. i, p. 333.

[25] Royal London Ophthalmic Hospital Reports, 1911, xviii, 198.

In the absence of more definite data concerning the character of the pigment it is futile to speculate as to the manner in which the eye structures become affected; at any rate, the study of cases of true hemochromatosis has still left the question of the formation and possible transporation of the pigment an open one. Since the publication of Wilson's observations and deductions, cases of this character will be watched with additional interest, and in turn it is hoped that in the study of certain clinical conditions already mentioned, the possibility of corneal pigmentation will be borne in mind.

From the study of these cases we can only conclude that in association with certain symptoms, of which a coarse intention tremor affecting the extremities and head is the most conspicuous, there may develop a deeply seated annular brownish-green pigmentation of the cornea. That some or possibly all of these cases are associated with a cirrhosis of the liver, which has been shown to exist in 2 cases. That during the course of the disease a glycosuria or a lowering of the sugar tolerance may develop. Accepting the autopsy findings in 2 cases and the neurological opinions expressed on the case whose history is here reported, the nervous manifestations are not due to multiple sclerosis.[26]

In conclusion, I gratefully acknowledge the courtesty extended by Drs. Mills, Spiller, and de Schweinitz for placing this patient at my disposal for clinical observation.

INFANTILISM.

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The name infantilism was coined by Lasègue, who designated by it the persistance of childish characteristics, physically as well as psychically, into adult life. With the increasing knowledge of various clinical pictures the term underwent modifications, having been circumscribed by different authors in varying ways. A great impetus was given to the studies of the various forms of retarded and checked development by the investigations of the functions

[26] Since this manuscript was forwarded to the editor, Rumpel (Deutsch. Zeitsch. Nervenheilkunde, 1913, xlix, Heft 1 u. 2, S. 54) has referred in detail to the character of the liver changes and the pigmentation. He believes the hepatic changes depend upon a faulty fetal development which results in a functional insufficiency that gives rise to disturbances of metabolism and auto-intoxication, and that this is responsible for the neurological symptoms. The pigmentation he regards as an argyrosis.

of the endocrine glands, which proved their great influence upon the physical and psychical growth. In connection with these studies, only the names of Hegar, W. A. Freund, Halban, Di Gaspero, and Anton may be here mentioned.

At present a general and a partial infantilism is recognized; yet a definite determination of infantilism against a number of other pathological conditions is at present not always possible. The term is not yet precise, and the various attempts at making subdivisions of this anomaly are not free from objections. Anton, with an attempt at an etiologic arrangement, gives a table of the various forms of infantilism, which in its modification by Dietrich is as follows:

1. Infantilism without detectable causes (genuine infantilism, primary defectiveness of the germinal cell).
2. Infantilism due to disturbance of inner secretions.
   - (*a*) Infantilism with myxedema and cretinism (thyreogenic).
   - (*b*) Infantilism with absence or underdevelopment of the genitals (dysgenitalism).
   - (*c*) Infantilism due to disturbance of the various visceral glands, as thymus, parathyroid, suprarenals, pancreas, etc.
3. Infantilism due to other internal disturbances.
   - (*a*) Infantilism in primary brain diseases.
   - (*b*) Infantilism in angioplasia.
4. Infantilism due to toxic and trophic disturbances.
   - (*a*) By intoxications of the parents (alcohol, lead, mercury, etc.).
   - (*b*) By congenital lues.
   - (*c*) By extra-uterine diseases, as f. i. intestinal catarrh, tuberculosis, valvular disease, pellagra, malaria.
5. Mongolism, Anton.

General infantilism, according to Anton's definition, is a disturbance of the development, characterized by a persistence of infantile or childish characteristics in the whole organism, preventing the development of the individual to the full extent of his species; not only the physical characteristics of childhood persist, but generally the psychical qualities also.

The principal features enumerated by most authors are: smallness, retarded or arrested growth of the skeleton and musculature, and corresponding smallness of all organs; underdevelopment or lack of the sexual organs, with that of the secondary sexual characters; finally the persistence of the psychic functions in the infantile or childhood stage.

However, we encounter various morphological as well as etiologic types of general infantilism, and in various degrees, varying from only slight development to the highest degrees of dwarfism. Infantilism is a morphological anachronism. When applied to the

early life, the term has only a relative meaning, of course, designating the persistence of size and characteristics of an earlier age.

Partial infantilism signifies the persistence of the infantile state in one organ or organ system or in the psychic functions. In the strict sense, also, general infantilism is only partial, inasmuch as there is perhaps never a complete congruence in the organs, their functions, the proportions of the parts, the psychic functions and the metabolism with those of infancy or childhood. A valuable contribution to the subject of partial infantilism was published by Tandler of Vienna in the *St. Paul Med. Jour.*, 1908.

Dysthyreogenic Infantilism. The type of general infantilism, to which attention was first directed, is the dysthyreogenic form, as we meet this frequently and most markedly as myxedema and cretinism. While the clinical picture of grave congenital or early acquired myxidiocy as an expression of athyreosis is familiar, it is equally important in view of the success of the organotherapy, to pay attention to the clinically abortive forms of myxidiocy, that are due to only a partial interference with the function of the thyroid gland, the hypothyroidism. Hertoghe pointed out the fact that between the "myxedème franc" (athyreosis) and the functional integrity of the thyroid there exist various degrees, some of which may be compatible with the intellectual requirements of ordinary life. To these forms he applied the term "hypothyrèoidie benigne chronique" or "myxedème fruste." We meet here all gradations from marked cretinoid habitus to the slight, hardly recognizable disturbances, which occasionally can be ascertained only *ex juvantibus*.

The "formes frustes" may present the cardinal symptoms of myxidiocy—namely, myxedema, dwarfism, and psychical disturbances—though in a milder degree and without imposing the stigma of physical and psychical degeneracy upon the afflicted.

They appear as individuals of more or less infantile exterior. Their habitus and size correspond to about the proportions of the newborn, in that they have a relatively larger head, round, fleshy face (full-moon face), a nose more or less saddled, and a stunted body. The navel may be low and the genitals are small and underdeveloped. The subcutaneous tissue is not firm, but doughy and flabby, although it seems at first sight similar to that of the infant; the skin is dry and scaly and the perspiration absent or scanty. The radiogram shows delayed ossification; the metabolism is subnormal. In the incomplete forms the face is expressionless, but less stolid than the extremely idiotic expression in athyreosis.

The intelligence is, as it seems, always affected, though occasionally only to a small extent; the apperceptive and thinking processes being heavy, slow, and clumsy. This is also seen in the inefficient or mediocre progress in school. However, the patients may learn reading, writing, and arithmetic, and may pass the elementary

school even with fair results in exceptional cases, as did, for instance, the two patients of Siegert. This would be impossible in athyreosis.

Even when there are only slight disturbances of the intellect, in the affective sphere they be more pronounced, inasmuch as the patients are rather apathetic, indifferent, and emotionless, as the monotony of the expression also demonstrates. Their muscular actions are slow and clumsy, as for instance, walking. Typical cases have been described and illustrated by Jannin, Magnus-Levy, Mennaches, Marfan and Guinon, Siegert, and others.

Siegert's interesting case concerned an eleven-year-old boy. There was myxedema with dwarfism, but a degree of mental development, incompatible with the complete picture of myxidiocy. He had passed even the entrance examination for the "Sexta" (High School in Germany). The correctness of this diagnosis was also confirmed by the splendid success of the specific therapy.

The following case is equally typical, and is remarkable for the splendid result of the organotherapy. This patient has been under my observation since January 17, 1911:

Emma F., of Norwood Park, a suburb of Chicago, (Fig. 1), born September 30, 1898. Parents, Germans, are farmers, healthy; no dwarfism, goitre, nor cretinism in the family. Breast-fed for fourteen months. The child learned to walk at eighteen months. Until the age of two years she was of normal size. She had obstinate constipation form the first, was always quiet and somewhat clumsy, and slow in her motions. She spoke rarely, but no other peculiarity was observed in her speech. The mother remembers that the child perspired around the nose in the summer. The child was always sensitive to cold and chilly, therefore she would crouch near the stove. Even in warm weather her hands and feet were cool, and looked bluish and marbled. She lacked the inclination to play and frolic around like other children, and is still awkward in dressing herself without help. At the age of six and one-half years she entered the public school, where she passed in reading and writing, with rather good results, but was poor in arithmetic. She learned little poems and prayers in the Sunday School without much trouble. When eleven years old her dentition corresponded to that of a child five years younger, according to the statement of a dentist. Her appetite had always been poor. The girl is at present in the fifth grade.

Status Præsens. January 17, 1911 (Fig. 1). Girl, aged twelve years and four months. Body length, 43¼ inches (instead of 58½); weight, 53 pounds (instead of 88 pounds). Head big, face round (full-moon face), somewhat puffy, and with a monotonous, cretinoid, "worried" expression. The nose is saddled and the forehead wrinkled; there are swellings of the subcutaneous tissue on the chin and in the region of the forehead, especially of the glabella and above the eyebrows.

The teeth are incomplete, many of them being absent. The tongue is not enlarged.

The integument in general is pale and dry, and on the arms, legs, and the lower parts of the trunk it is rough.

There are moderate swellings of the subcutaneous tissue above the clavicles, over the pectoralis muscle, in the lower part of the abdomen and more markedly on the mons Veneris. The hands and feet are cool, with their dorsal surfaces distinctly puffy, and the skin of the arms and legs is marbled (cutis marmorata). The thyroid gland is not palpable. The abdomen is protruding; there is no umbilical hernia. The intelligence corresponds to the anamnestic data.

FIG. 1.—Hypothyreogenic infantilism before thyroid treatment.

FIG. 2.—Same case as Fig. 1, after thyroid treatment.

Diagnosis. Forme fruste of myxidiocy (hypothyrogenic infantilism, type Brissaud).

The diagnosis was confirmed by the remarkable effect of the thyroid therapy. I saw the child repeatedly and the gradual changes were easily seen.

April 17, 1911. The child measured 45½ inches in height (an increase of 2¼ inches in three months), although the body weight was one pound less than before treatment.

January 7, 1912. The length was 49 inches (an increase of 5¾ inches in one year).

April 30, 1912. Length, 50¼ inches.

August 3, 1912. Crines pubis are appearing on the labia majora.

September 30, 1912. Patient grew the last month ¾ inch; measures 52 inches; this means a total growth of 8¾ inches within nineteen months.

She is a healthy-looking, red-cheeked girl, and helps assiduously in the daily housework. The arms and legs have still a tendency to be cool and marbled, and the child is still sensitive to cold. The excellent effect of the thyroid therapy, which was periodically interrupted, was evident by the pronounced acceleration of the growth, which surpassed the normal ratio within this period of time, by the disappearance of the subcutaneous swellings, by the more intelligent expression of the face, by the eruption of many teeth, and by the improvement of the psychical backwardness, in the disappearance of the torpor, which was replaced by normal quickness. The abdomen became less prominent, the defecation regular. How much the type was changed after three years' treatment with thyroid is well demonstrated in Fig. 2.

Dysgenital Infantilism. As is well known, a disturbance of glands other than the thyroid may also retard normal mental and psychic growth. Numerous researches into the function of inner secretion prove the importance of harmonious correlation and equilibrium among the various endocrine glands for the normal development of the whole organism and its parts.

Thus one series of cases of infantilism originates from a disturbance of the sexual glands. They exert an important influence upon the organism, to a certain extent even before puberty, as the common experience of stock breeders shows. The normal growth, the sexual impulses and potency, and the full development of the secondary sexual characters depend upon the functional integrity of the interstitial tissue, that is, the Leydig cells of the testicle and the corresponding cells of the ovary.

Tandler and Gross, for instance, observed in male deers the development of rudimentary antlers (Perückengeweih) only after castration, but not after the experimental destruction by *x*-rays of the generative part of the testicles, thus leaving the inner secretory interstitial cells unaffected.

Castration in young boys doubtless is rare, but the testicles may be completely destroyed by congenital luetic processes (castratio subalbuginea, Scringe) that are identical in their effect. Observations on man could be made profitably among the various people who practise castration, for example, the Skopzes in Russia or the eunuchs in the Orient.

The type of infantilism caused by a defective function of the sexual glands is termed dysgenitalism. The patients thus afflicted may be called eunuchoids, a term coined by Tandler and Gross in Vienna on account of their resemblance to the eunuchs. Other

terms used in the literature are infantilism avec gigantism, dystrophia adiposogenitalis, geroderma genitodystrophico.

The dysgenitalism may present itself in two differing principal types: gigantism and adiposity, although transitional forms exist.

In the dysgenital giants of the first group we meet the following features: the period of growth extends beyond the normal time, occasionally even beyond thirty years of age. This abnormal increase of length affects especially the lower extremities, resulting in the characteristic "eunuchoid" longleggedness. The epiphyseal cartilages remain unossified beyond the normal limit of time, in some cases even beyond the age of thirty years, which condition can be demonstrated clinically by the *x*-rays. The genital organs are only slightly or not at all developed, and the secondary characters are absent or only suggested.

These types, that is, gigantism and dysgenital adiposity, are both encountered among eunuchs and also among the Skopzes in Russia. Tandler, in a number of cases, found an enlargement of the hypophysis cerebri, the sella turcica in the *x*-ray picture being enlarged and deepened. This enlargement of the hypophysis together, with the genua valga, found in dysgenital gigantism as well as in acromegaly, has led Brissaud, Meige, and others to assume a certain relationship between gigantism and acromegaly. In fact, giants have been observed in whom later acromegaly supervened.

The abnormal persistence of the epiphyseal cartilages is considered a consequence of inhibition of the inner secretion of the sexual glands, and this condition is necessary, of course, for an increase in length, which will result where hyperactivity of the hypophysis is present. When the epiphyses are ossified the result of hyperactivity of the hypophysis will be acromegalic growth only.

In dysgenital adiposity the second clinical form of dysgenitalism, a lack of development of the sexual organs and the secondary sexual characters is likewise present. The larynx remains small and cartilaginous even late in life. There exist also longleggedness, though less pronounced, and a retarded ossification of the epiphyseal cartilages and genua valga. The pelvis resembles that of a child or a castrate. The chief difference between this condition and gigantism is the presence of abnormal adipose tissue, occasionally increased to a marked degree, and in special localizations that are characteristic of genital origin. The mammary regions especially have deposits of abundant adipose tissue to such a extent that they may take on the appearance of female breasts. Furthermore, exaggerated deposits of panniculus adiposus are located in the regions of the hips and ad nates in the lower region of the abdomen, and on the mons Veneris, which may be separated from the suprapubic fat by a deep furrow, as in children. A high-pitched voice and beardless face complete the picture of feminism.

The face is sallow, the skin soon becomes wrinkled and senile, therefore this affection is named also geroderma. Tandler and Gross found that the thymus persisted an abnormally long time in many cases. The *x*-ray examination showed the hypophysis cerebri was usually not enlarged.

The connection between the above-described characteristic type of adiposity and disturbances of the germinative glands is experimentally established as a fact by castration of animals and man. In addition to this, we find in castrates and in eunuchoids very early a penetration of fat tissue into the musculature as in castrated animals.

It must be remembered, however, that this whole problem is rather more complicated than it seems at first sight, being entangled by numerous phenomena due to the correlation and simultaneous functional disturbances of other glands of internal secretion. I only point here to the fact, that, although increased length is the rule among the eunuchoids and Skopzes, in some individuals only normal, subnormal, and even small measurements are observed. Eunuchs and eunuchoids, although similar, are by no means identical, and data by experimental castration should be only applied with great caution in explaining eunuchoidism, in which the sexual underdevelopment may be only a part of a general abnormity. It is not yet explained, also, why in one case primary dysgenitalism leads to gigantism, in the other case to adiposity. Tandler and Gross reported only male eunuchoids; female eunuchoids have been reported lately by Peritz, Wolff, and Hutchinson.

Pituitary Eunuchism. A clinical type of adiposity, similar to that in dysgenitalism, is also found accompanying pathological processes of the hypophysis cerebri, in the so-called hypophyseal adiposity or pituitary eunuchism.

Since Froehlich, who in a case of tumor of the hypophysis observed adiposity and underdevelopment of the sexual glands in addition to the tumor symptoms, has emphasized the diagnostic importance of the first symptoms in hypophyseal affections, this type has been repeatedly seen and verified by postmortem or during operations (v. Eiselsberg, Frankl Hochwart). When it develops in boys or youths the external sexual organs remain in an immature state, the perigenital hairs are scanty and have boundaries of the feminine type, the beard is absent, the skin is delicate and hairless, and the voice is high-pitched—in short, the secondary sexual characters are not normal. In addition to this, adiposity is a prominent feature, striking by its eunuchoid localizations more than by its degree, thus giving the individual an appearance of feminism like in eunuchs and dysgenital eunuchoids. In most cases the size of the body remains below the average; also dwarfism has been observed. These facts deserve special attention in respect to the relationship between hypophysis and growth of

body. The symptoms are of course less pronounced, when starting after maturity.

Many varieties, deviating in various degrees from this classic type do occur, but without completely obliterating the original. Hypofunction of the pituitary gland (hypopituitarism) is responsible—possibly directly, according to the views of some authors, or indirectly according to others, as Schüller and Tandler, etc., who maintain that the dystrophic adiposity take place only when the disturbance of the hypophyseal function entails a disturbance of the germinative glands, that is, Leydig's cells.

Although in pituitary adiposity mostly lesions of the hypophysis (tumors) are to be found, in a number of cases no palpable anatomical lesions of the hypophysis were present. Many other problems of this complex subject being unsolvable as yet, the question arises whether we have to deal in such cases with a primary eunuchoidism or secondary eunuchoidism, in which the pituitary gland, although apparently anatomically normal, may functionally be deficient, thus exerting a detrimental influence upon the development and function of Leydig's cells.

Endogenic adiposity of enormous degrees has been observed in childhood as early as in the first two years of life. While we may ascribe it to hypothyroidism, accepting the views of Hertogh, who regards it as an attenuated form of infantile myxedema, we also have to acknowledge in some instances of adiposity in children hypopituitarism as the causative factor since the studies of Frankl Hochwart, Froehlich, Madelung, Marburg, and others. But perhaps it is the insufficiency of the inner secretion of the germinative glands—an imperfect or delayed formation of Leydig's interstitial substance—which is more often responsible for adiposity during the age of prepuberty, in boys especially, who show the eunuchoid localizations of the adipose tissue. This adiposity may be either only temporary or permanent.

After these considerations we will outline here the history of the following case, that will lead to a further discussion as to the possible pathogenesis (Figs. 3 and 4).

Wilhelm M., of Chicago, aged twenty-one years, one month; parentage, German. Family history, negative. As a child he developed in an entirely normal way mentally and physically. A photograph taken when he was five years old corroborates this statement of his parents. He was entirely healthy until about eight years old, when he suffered from typhoid fever, accompanied by delirious states; this kept him in bed for about two months.

A remarkable retardation of his longitudinal growth dates from this time. This was accompanied by a gradual, slow increase of the adipose tissue that attained a striking degree. For the following six years he suffered from cephalalgia, which was at first only slight, but later intense and almost daily.

A photograph of the boy in his fourteenth year, with a group of his classmates, demonstrates by comparison the pronounced change, to wit, alteration in the body form, the striking shortness, and adiposity. Crines pubis since about four years. No libido; coitus and masturbation denied; during the last year pollutiones nocturnæ at long intervals; erections rare. Patient asserts that his perspiration is scanty even after exertions, and that he is easily chilled in cool weather. The intelligence is good.

FIG. 3.—Eunuchoid localizations of adipose tissue.

FIG. 4.—Dorsal view of Fig. 3.

I saw the boy the first time on September 25, 1911. The status præsens was the following: Patient was aged twenty-one years, two months; 57⅞ inches high, the size of a normal thirteen-year-old boy. Weight, 133 pounds (average weight of a thirteen-year-old boy is 84.67 pounds). A much increased flabby panniculus adiposus, with special localizations of predilection, as in the mammary regions, that have a more or less feminine form (as seen in Fig. 3), above the clavicles, under the chin (double chin), on the abdomen especially in its lower part; therefore it is prominent; on the upper arms, thighs, hips, ad nates, and on the mons Veneris, which is separated from the abdominal adiposity by a furrow, somewhat

as in a child. These eunuchoid localizations, together with the broad hips and slanting shoulder lines, give the man a body type similar to the female, even if seen from behind as Fig. 4 demonstrates. The head is big and the face full, but with an immature, infantile expression. There is only the slightest suggestion of a beard or mustache. The axillary hairs and crines pubis are well developed, the latter, however, being of the feminine type in their boundary. The larynx is small and without projecting thyroid cartilage. The voice is high-pitched, so that, when talking over the telephone, he is often mistaken for a little boy or girl, as the patient himself admits. The hands are small, graceful and feminine. The *x*-ray picture of the hand shows the epiphyseal cartilages of the phalanges and metacarpals not yet ossified. The sella turcica in the *x*-ray picture of the head seems to be of normal shape and size. It is impossible to palpate the thyroid on account of the adipose tissue.

Genital Organs. Penis short, somewhat smaller than normal, and deeply buried under the cushion of the adipose tissue of the mons Veneris; the scrotum is of normal size, the testicles also of about normal size, but drawn high up within the scrotum; the prostate gland is small.

Intelligence and memory are good; patient is musical, good-natured; but immature in his character.

MEASUREMENTS OF THE BODY.

Body height	57¾ inches
Circumference of the head	22 "
Broadness of the shoulders	16 "
Stretch of arms	58½ "
Circumference of the chest at the level of the mammæ	36 "
Circumference of the abdomen in the level of the epigastrium	32 "
Circumference of the abdomen in the level of the umbilicus (umbilicus is low, only 2 inches above the horizontal line of the cristæ ossis ilei)	37½ "
Distance of the umbilicus from the processus xiphoideus	8¼ to 9 "
Distance of the umbilicus from the symphysis	5½ "
Distance of the symphysis from the floor	28 "
Circumference of the thigh at the level of the perineum	22 "
Circumference of the upper arm	12½ "
Distance of the cristæ ossis ilei	10¾ "

There is no doubt that in this case a disturbance of inner secretion, due probably to typhoid infection, is the underlying cause. This is evident from the small size of the patient, the eunuchoid adiposity, the non-ossification of the epiphyseal cartilages at the age of more than twenty-one years, certain anomalies in the sexual sphere form the lack of the normal development of certain secondary characters, accompanied by a certain degree of immaturity of character.

The scanty perspiration, chilliness, and universality of the adiposity would suggest a participation of the thyroid. However, the failure of the thyroid therapy to influence these conditions

militates against this assumption. On the other hand, disturbances of the function of the skin are known to exist in affections of the hypophysis, as hyperhydrosis in acromegaly and scanty perspiration in hypopituitarism.

Progressive obesity has been observed not infrequently after typhoid, due to its deleterious effect upon the thyroid. Von Noorden mentions two such cases and quotes another, where a strumitis during typhoid was followed by obesity and a few years later by myxedema. We encounter several similar instances in the French literature. But in a number of cases the adiposity after infections was due to an involvement of the pituitary gland by meningeal processes, as they are observed in pneumonia, scarlatina, typhoid, etc. Indeed, my case offers some features that Neurath observed in one of the cases, that he described and illustrated under the title "Fettkinder" (obese children). That case was the following:

Boy, aged ten years; after scarlatina, when seven years old, there developed an enormous, monstrous adiposity; the growth was remarkably retarded and the boy suffered from attacks of headache and vertigo. The boy's size, 109 cm., corresponded to the size of a normal boy of six years of age, while his weight was 36.8 kilos, corresponding to the body weight of a thirteen-year-old boy. Circumference of the head, 53 cm. The testicles were well developed; the penis was hidden in the adipose tissue of the mons Veneris. The *x*-ray examination of the skull demonstrated signs of hydrocephalus to some degree, but a normal sella turcica. Neurath asserts an affection of the hypophysis in this and similar cases, caused by a hydrocephalic effusion due either to meningitis serosa accompanying scarlatina or to a small tumor that could not be detected by the *x*-rays.

In analogous cases, as for instance those reported by Marinesco and Goldstein, Babonneix and Paisseau, Krueckmann and Meyer, and Kurt Goldstein, the pathogenic factor was a pressure lesion, with consequent hypofunction of the hypophysis through hydrocephalic effusion that distended the third ventricle, calling forth symptom pictures of pituitary adiposity.

It is an interesting and important fact that extirpation of the hypophysis in animals has resulted in adiposity, resembling degeneratio adiposogenitalis in man (Cushing, Aschner).

Retardation and cessation of growth, caused by hypofunction of the pituitary gland, is known by clinical observation as well as by animal experiments. Among others, Babinski found in a seventeen-year-old girl a tumor of the hypophysis as the sole explanation of the syndrome of infantilism, and Benda reports a a case of pronounced dwarfism combined with a complete destruction of the hypophysis by a tumor, consisting of hyaline tissue, osseous trabeculæ, epithelial cells, and cholesteatoma masses.

Among the patients of Marinesco and Goldstein, Kurt Gold-

stein, Babonneix and Paisseau, some are of a strikingly small size and have large heads. In one of the cases of Babonneix and Paisseau the morbid adiposity started after scarlatina, as in the case reported by Neurath. We may infer from these various reports that this type of pituitary adiposity in children may occur with or without a clinically demonstrable disturbance of the genital organs (dysgenitalism). Biedel, among 32 cases of hypophysary adiposity, found only twelve with genital atrophy, and states that in the beginning of the affection a genital involution cannot always be found.

In the light of the above observations the case described by me possibly may be classified under the category of cases of pituitary adiposity as exemplified by the case of Neurath above quoted.

The intense headaches since the typhoid would argue in favor of a possible meningitis serosa during his disease, though unfortunately no more exact data than the vague statement that the patient was for some time delirious could be had as to the course of the typhoid. The lower reflexes are not increased. Among other points the lack of longleggedness speaks against a primary (partial) dysgenitalism. The symptoms in the sexual sphere with the undervelopment of some of the secondary sexual characters then would be secondary, induced by a disturbance of the hypopysis.

Pluriglandular Infantilism. In myxedematous infantilism the athyreosis is the principal but not exclusive factor, the function of other endocrine glands being more or less involved. Atrophy of the genitals, atrophy, interstitial inflammation and abnormal persistence of the thymus (Sainton and Rathery), hypertrophy (L. Meyer Aschoff), atrophy with cystic degeneration (Pontif) of the hypophysis cerebri, and atrophy of the adrenals have been observed. In fact, according to the views of Sante de Sanctis, the whole system of the endocrine glands is involved.

Gougero and Claude devoted careful studies to the subject of "insufficance pluriglandulaire endocrinienne." By this term is understood the symptom-complex of insufficiency of a number of endocrine glands, as of the thyroid, testicles or ovaries, adrenals, hypophysis, etc.

As the associations of pluriglandular insufficiency are various and of different degrees, it is plain that there does not exist only one syndrome but a series of syndromes, varying according to the glands affected, the degree and succession of the disturbance of each single gland, and the age of the person.

Claude and Gougero bring the history of an instructive case of pluriglandular insufficiency concerning a forty-nine-year-old man. An alcoholic, with chronic tuberculosis of the lungs and lymph-glands. During convalescence from acute nephritis there appeared symptoms that rendered the case interesting, namely loss of the genital functions, loss of the secondary sexual characters, as loss

of beard, axillary hairs, pubes, change of the voice; atrophy of the testicles and the penis; a syndrome indicating insufficiency of the sexual glands; chilliness, dryness, and desquamation of the skin; an old, wrinkled face; atrophy of the thyroid; psychical decline; emaciation; asthenia; in the last months pigmentations of the skin and a striking decrease of the arterial pressure, which was interpreted as suprarenal insufficiency. The insufficiency of the thyroid, testicles and suprarenals, recognized during life, was verified by autopsy and histology, which in addition revealed lesions of the hypophysis, pancreas, parathyroid, kidneys and liver.

The authors collected from the literature a number of similar cases, described under various names, as those of Rumpel, Dalchè, Sainton and Duprè, Brissaud and Bauer, Gandy, etc.

In the young, pluriglandular insufficiency must needs result finally in infantilism, since the three glands which control the growth, namely, thyroid, sexual glands, and hypophysis, are involved.

A transitional case from primary dysgenitalism to pluriglandular insufficiency is reported by Peritz; interesting cases of pluriglandular infantilism were reported by Richon and Jeandelize, by Peritz, Nazari, Campioni, and others. In Nazari's case there were present infantilism, tuberculosis of the lungs and meninges, a cystic degeneration of the hypophysis, persistance of the thymus, hypoplasia of the thyroid and testicles.

As yet the clinical differentiation of pluriglandular infantilism from Lorain's type might be occasionally impossible, and perhaps by further studies some of the groups of Lorain's type will have to be classified among the groups of pluriglandular infantilism.

Dystrophic Infantilism. The type Lorain differs morphologically and etiologically from the type of Brissaud, exemplified by the first case of my series. Lorain described in 1871 the dystrophic type of infantilism, named after him. The individuals affected by it are small but graceful in contradistinction to Brissaud's hypothyrogenic type; they have "elegant, fine" forms; the extremities are long, the abdomen is not prominent, the adipose tissue not increased; the contours of musculature and skeleton are therefore not masked. It is true the genital organs are small, but they may be proportionate to the body. The intelligence is mediocre, small, childish, like the body. This type resembles *un homme miniature*, and presents, as Meige tersely says, the picture of a normal individual, seen through the opera-glass reversed. The aspect, therefore is that of one approaching puberty rather than that of an infant. The following case is an example (Fig. 5).

Charles H., of Chicago. Parents and two sisters healthy; no dwarfism; no lues; no alcoholism; nor abortus. The patient is the first child, born, allegedly, six to seven weeks before full term. Mother, then aged twenty-seven years, suffered from repeated attacks of acute rheumatic polyarthritis during the pregnancy.

At birth the boy was small and puny; the physician estimated the weight as 2 pounds, evidently an underestimate. Eyebrows and nails at birth were absent or hardly visible. For eight weeks the baby was kept wrapped in cotton near the stove, in order to be saved. Breast-fed for thirteen months, though always dyspeptic and diarrheic during this time. First teeth at the end of the first year; at sixteen months his weight was only 10½ pounds; at this time he learned to talk. He walked when twenty-two months old. At two years he was so small that he was demonstrated before an audience of physicians in St. Luke's Hospital as a curiosum. Afterward he was always sickly: he had chicken-pox, whooping cough, with a hernia as a sequela, existing for two years, severe scarlatina, and repeatedly bronchitis. At eight years he entered school, where he was backward. During the last two years he made mentally and physically comparatively great progress. However, at present he is only in the third grade of the public school, although twelve years and four months old. Thyroid therapy for five months, three years ago, had no effect whatsoever.

Status Præsens. August 11, 1912. Boy, aged twelve years four months. Size, 50½ inches (normal for this age, 55.4 inches). Weight, 42 pounds (normal, 76.9 pounds). Thus this boy is the size of a normal nine-and-one-half-year-old boy, while the weight is that of a five-and-one-half-year-old boy. The child has a healthy look and small, graceful stature. The skeleton is delicate and the musculature and panniculus adiposus is poorly developed. The skin is delicate, smooth, and moist, with a good, healthy, and abundant growth of hair on the scalp. No swelling of lymph glands. The head is markedly dolychocephalic (cephalic index, 67.8). The face is long and narrow. The teeth are normal and in good condition. Internal organs normal. Diastasis of the musculi recti abdominis. The medial lobe of the thyroid distinctly palpable; the lateral lobes not with certainty. Crines pubis limited to around the root of the penis; the right testicle is small, of the size of a bean, 1 cm. long, instead of olive sized for this age. The left testicle is slightly smaller than the right one, and is retained in the inguinal canal, but can be drawn into the scrotum. The penis is only 1¼ inches long, with the glans broad and thick. The mental development is backward, perhaps about as much as the physical.

FIG. 5.—Lorain's type.

MEASUREMENTS OF THE BODY.

Height	50½ inches
Head: Circumference	18½ "
Bitemporal diameter	3¼ "
Biparietal diameter	4½ "
Frontoöccipital diameter	6⅝ "
Mentoöccipital diameter	8 "
Circumference of the chest at rest in mammary line (normal 24½ inches)	21 "
Breadth of shoulders	10½ "
Stretch of arms	48½ "
Distance of the symphysis from the floor	26 "
Distance of the cristæ ossis ilei	7½ "
Circumference of the abdomen in umbilical line	18¼ "

The following case deserves to be mentioned here because its prenatal history is similar to that of the foregoing case:

Mamie B., the second among four children, born at full term. Mother suffered during this pregnancy from severe rheumatic polyarthritis, which kept her in bed for almost eight months. The girl was at birth very small, weighing, by report, only one and a half pounds; breast-fed for one and a half years, with the addition of other food after the first year. First teeth at eight months; learned to walk at one year and three months and to talk in the third year. She has always been healthy, but suffered last year for some time from enuresis nosturna.

Status Præsens. Girl, aged six years nine months, healthy looking, but very small. Body weight, 29½ pounds (weight of a normal girl two years old). Height of body, 39⅝ inches (size of a normal girl two and a half years old). Circumference of chest only twenty inches. Fronto-occipital circumference of head, twenty inches. Distance of symphysis from floor, 19⅖ inches. Body graceful, well proportioned, panniculus adiposus and musculature poorly developed. Teeth complete, in very good condition. Skin smooth, of healthy color, so also the mucous linings. Abdomen somewhat prominent. Urine normal.

Though the morphological type of Lorain is unmistakable and characteristic in its pure form and differing from Brissaud's type with its more or less infantile somatic attributes, yet occasionally it may in forms not well marked be difficult to differentiate them clinically in the young. In such cases the anamnesis and thyroid therapy will be helpful, Brissaud's dysthyreogenic type showing a rapid and decided improvement.

It is not surprising that combinations of both types occur, since the etiologic factors causing dystrophia may be complicated by hypothyroidism, as in the interesting case of Duprè and Pagniez.

Etiology. In the etiology of dystrophic infantilism, factors which call forth a debility of the whole organism come into consideration. This form is encountered sometimes accompanying the status lymphaticus and as a consequence of chronic infections;

above all, either in lues hereditaria or in lues aquired very early; in descendants of parents who are suffering from tuberculosis, chronic alcoholism, pellagra, malaria, leprosy, or other endemic diseases; in persons with congenital or early acquired valvular disease, particularly with mitral stenosis (nanisme mitral) or pulmonary stenosis. It is found also in individuals showing only malnutrition and poor unhygienic social conditions as causative factors. The infectious diseases mentioned may be active either through devitalizing and debilitating the germinative organs and germ cells of the parents, or the children themselves may be affected.

In both of my above reported cases severe rheumatic polyarthritis was present in the mothers during gestation; therefore I am inclined to consider this infection as a factor that had some bearing upon the anomaly in the newborn.

Children who have long suffered from severe tuberculosis in any part show often signs of retarded development, and spinal caries is a comparatively common cause of this retardation (Marie and Leri, "infantilisme pottique").

According to Hertogh's views, the thyroid would hold a central etiologic position even in the presence of these causes, inasmuch as only a preëxisting disturbance of the thyroid function or one provoked by these agencies (lues, tuberculosis, etc.) could bring into existence an infantilistic stunting of growth. However, this exclusive standpoint can no longer be maintained in the face of clinical evidence. As Ferranni has pointed out, many cogent reasons argue against Hertogh's extreme standpoint.

The dependency of dystrophic infantilism upon malarial infection is evident from its comparative frequency in malarial districts.

Ferrannini, in Sicily, and H. de Brun, point to the numerous emaciated dystrophic individuals of small figures and senile countenances among those who have suffered from malaria in early life. I made similar observations in Syria.

Differing from the pure type of Lorain, these persons have an enormous abdomen, due to the intumefaction of spleen and liver. Grotesque figures result from this contrast of general emaciation and enormous abdomens.

Orgeas shows us the stunting effect of parental malaria upon the offspring of Europeans in French Guiana. He emphasizes the extreme smallness of the body, the flabby skin, the atrophy of the male genitals, and microcephaly as main features of these "variations morbides." This degeneracy of the children, especially the males, due to chronic malaria and deterioration of the parents, is one of the chief causes of the extinction of the unmixed white race in the tropical (malarial) lands.

Another factor, causative of dystrophic infantilism, is chronic disturbance of the gastro-intertinal tract, with consequent malnutrition and cachexia.

However, we must not lose sight of the fact that infantilism itself from any cause may predispose to intestinal insufficiency or to other diseases, as tuberculosis, forming thus a vicious circle.

Babies with poor digestion and assimilation remain puny and meager for long time, and their mental growth is retarded also. Fortunately this delay in most cases is only temporary. But in more severe cases the affected individuals remain small, puny, dystrophic in the full sense of the term. One also observes this occasionally among those prematurely born, especially if nourished insufficiently and artificially.

Herter, in a monograph (1908), describes several children, all underdeveloped, due to intestinal disturbances with a characteristic intestinal flora, (Baccillus bifidus Tissier and Bacillus infantilis), and similar cases are reported by Freeman, Heubner, and Schulz.

M. Landolfi reports an interesting case of infantilism of gastric origin. The patient, aged twenty years, was the size of a ten-year-old boy; the stunted growth was due to gastrosuccorrhea of long standing.

In addition to the etiologic factors mentioned so far, affections of various other parenchymatous organs have been accused as the cause of infantilistic forms (*vide* table of Anton).

Byron Bramwell describes a case as infantilismus pancreaticus. Male, eighteen and one-half years old, with the aspect of an eleven-year-old boy. The epiphyseal cartilages still unossified. The cause of this inhibition of growth was a chronic diarrhea for nine years. Under treatment with pancreas for two years, the boy grew $5\frac{7}{8}$ inches and gained $23\frac{3}{4}$ pounds; the sexual development became normal.

A similar successfully treated case is recorded by J. L. Renroul.

Morlat reports an observation of infantilism produced by insufficiency of the suprarenals, with great improvement by administration of suprarenal extract. Thyroidin was ineffective.

The dependency of the sexual function upon the suprarenals is well known from its disturbance in Addison's disease. Tandler found in cases of Addison's disease alterations of the interstitial cells and in the germinative part of the testicles, and similar changes in the testicles of a man with primary hypoplasia of the suprarenals. Wiesel and Karakascheff and others describe retardation of the sexual characters in hypoplasia and atrophy of the adrenals. The case of Recklinghausen is even more convincing, since in the above cases one might consider the hypoplasia of the adrenals and genitals as coördinate symptoms, due to a common cause. Recklinghausen's case concerned an eighteen-year-old dwarf, 95 cm. in height, $10\frac{1}{2}$ kilos in weight, with the appearance of a four-year-old boy. The postmortem revealed caseous inflammation of both adrenals. Recklinghausen considers the possibility of a connection between dwarfism and degeneration of the suprarenals.

It might not be amiss here to point to the connection between premature sexual development in children as early as from one to seven years of age, and the adrenals. From the literature one may gather that a sudden and rapid genital and general physical development with secondary sexual characters in young children was encountered especially in those cases, that showed at autopsy tumors of the adrenals and kidneys (hypernephroma) (Bulloch and Sequeira).

Finlayson gives a report of a twenty-three-year-old man, who suffering from biliary liver cirrhosis, had a weight of only 35½ kilos. His brother, aged nineteen years, likewise suffering from biliary liver cirrhosis, had a weight of 31 kilos.

Hasenclever published three cases of infantilism suffering from liver cirrhosis. Additional cases are reported by Gilbert and Fournie, Lereboullet, Cautley, and others.

Otto May speaks of renal infantilism in congenital or early acquired affections of the kidneys, chronic interstitial nephritis and diabetes insipidus. (Miller and Parson, Fletcher, A. Naish, Miller, Sutherland.)

Weber and Cherry contribute observations pertaining to this category of infantilism.

Finally, also primary disturbances of the brain, as encephalitis, porencephaly, microcephaly, paralysis progressiva in early life exert an inhibitory, detrimental influence upon the development of the whole body.

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STUDIES ON THE SMEGMA BACILLUS

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PART I.—LITERATURE.

Introduction. Closely following the discovery of the tubercle bacillus by Koch, in 1882, other workers announced the finding of bacilli resembling the tubercle bacillus in staining and morphological characteristics. Several claim credit for this discovery—all working and reporting at about the same time—chief among whom are Alvarez, Czaplewski, Doutrelepont, Laser, Matterstock, and Tavel. Only one year earlier, in 1884, Koch had suggested the idea and possibility of there being several other bacilli with staining properties similar to those of the tubercle bacillus.

Smegma Bacillus. This newly discovered bacillus—the smegma bacillus or Bacillus smegmatis—came in apparent answer to this prophecy, and was doubly confusing because it resembled the tubercle bacillus not only in its chief and heretofore distinctive characteristic—its staining properties—but also in its morphology. This confusion and difficulty were likely to be encountered in bacteriological examinations of urine where mistaken diagnoses have probably resulted in many useless but serious operations.

We are indebted to Dr. M. P. Ravenel, director of the laboratory, for assistance and advice during the progress of this work and in the preparation of this paper.

The work divides itself into two main parts: (1) a study of the available literature, which is scarce as well as conflicting, and (2) the laboratory work.

Occurrence. The smegma bacillus is found widely distributed over the surface of the human body. It appears in especially large numbers in any place where the normal skin secretions are allowed to collect, as about the genitalia, under the foreskin in males, and between the labia in the female, about the anus and the perineum of both, in the umbilicus, in the cerumen of the ear, about the teeth, etc. In this respect its occurrence is dependent upon the degree of cleanliness of the patient. It also appears in the urine—more abundantly in females—where, according to some writers, it may be found in 59 per cent. of the cases, while others report it as rarely present, especially in urine from males. It has also been

reported present in sputum and lung cavities in cases of gangrene of the lungs and fetid bronchitis. One case has been reported of an ovarian cyst in which bacilli very similar to if not identical with the smegma bacillus were found, which were thought to have been there by perforation from the rectum or by digital examination.

The occurrence about the genitalia and possibility of gaining entrance into the urine, where they might be mistaken for tubercle bacilli, resulting in a diagnosis of genito-urinary tuberculosis, forms the chief point of practical consideration in the study of the smegma bacillus. This source of contamination of urine, however, is not deep-seated, since no writer reports finding smegma bacilli in the bladder or the deeper portions of the urethra. On the other hand, several report unsuccessful attempts to find them there.

One investigator reports work done on animals in which he found the smegma bacillus about the genitalia of horses, dogs, cattle, guinea-pigs, and white rats. The cat and rabbit gave negative results. In smear preparations, several note the tendency of the bacilli to be found more abundantly in and about epithelial cells or other debris.

MORPHOLOGY. The difficulty and uncertainty of cultivation necessitate greater dependence on microscopic findings, but it is here that we find the close resemblance of the smegma bacillus to the tubercle bacillus, and morphology presents one of the two chief possibilities of confusion.

It varies widely in morphology, but usually is 3 to 5 μ long by $\frac{1}{4}$ to $\frac{3}{4}$ μ wide: a rather long, slender, often slightly curved bacillus or little rod with rounded ends. Its morphological variations seem no more limited to one dimension or property than to another. It may be about the same length as the tubercle bacillus as ordinarily found in human sputum—much shorter, much longer—or we may find some preparations with only straight bacilli, or others almost entirely composed of small curved rods, some thicker, some thinner. The short bacilli often appear like comma bacilli. Some authors claim the form and size are dependent on the kind of culture media used. One author suggests that the degree of curvature is apparently dependent on the position of the bacillus in the colony—those nearest the centre being most curved, while those farther out and composing filaments are straight. A wider variation from cultures is only to be expected from, and certainly would tend to strengthen the doubt in, the fact that the organism has not yet been cultivated, at least not so frequently and generally as claimed.

Dahms claims never to have found a "smegma bacillus showing in a typical way the peculiar sharp curve near one extremity which is so frequently observed in tubercle bacilli."

Many claim to have found so-called "spores," "spore bodies," "sporogenic bodies," etc., appearing at each end of the stained bacillus, taking a deeper stain and giving to short bacilli at least

the appearance of diplococci or of two cocci lying close to each other. Preparations from colonies on media producing rapid growth show evidence of manner of growth and development. Scattered among the bacilli throughout the field are to be found numerous short, oval segments or egg-shaped bodies of the same color as the bacilli, but quite separate and distinct from them. Also other bodies—little rods intermediate in size between the egg-shaped segments and the mature bacilli—are found and seem to be an intermediate stage of development. Some report finding granular bacilli on certain kinds of media, especially Löffler's blood serum, while others claim never to have seen granular forms. Hang-drop preparations show absence of independent motion.

STAINING. Staining is the second important point in which the smegma bacillus resembles the tubercle bacillus, and this is second in order of enumeration only, because in order of importance it really holds first place. Like the tubercle bacillus, the smegma bacillus belongs to the class of so-called "acid-fasts," *i. e.*, it resists decolorization by acids after staining with carbol-fuchsin. Herein lies the real difficulty for the clinician, for the test long held for the tubercle bacillus was this property of acid-fastness. Then the discovery of the smegma bacillus introduced a source of error in that in certain cases, as for instance in the examination of urine for tubercle bacilli, the mere finding of red bacilli after decolorization, was not sufficient basis for diagnosis of genito-urinary tuberculosis, because it might be the smegma bacillus. Immediately several workers undertook the problem of devising a method whereby an accurate differential diagnosis could be made between these two similar organisms, and their attempts, especially those of the earlier workers, were to stain it under two conditions: in tissue and in smear preparations.

These efforts proved successful in quantity but of doubtful success in value, since scarcely any two workers have reached the same conclusions. Yet each has proposed and enthusiastically advocated some method quite different from all others, and one which he is sure will prove reliable in all cases at all times. As a rule, he has been equally enthusiastic and urgent in his disapproval of all other methods of differentiation by staining or otherwise. At the present time no absolutely reliable method of differentiation by staining properties has been found, and yet more than twenty different methods have been advocated by the originator of each. The cause of this wide variation in results is found primarily in the variable staining properties of the smegma bacillus, and possibly secondarily in the fact that no one observer has done sufficiently extensive work to prove the inaccuracies of his own method. More recent writers suggest the impossibility of a differential method of staining due to the variation in the staining reactions of the smegma bacillus and its close relationship to the tubercle bacillus.

The numerous methods thus far suggested have, in the main, agreed upon and been based on two points: (1) that the smegma bacillus stains with difficulty but is equally slow and difficult of decolorization, and (2) that it possesses both these properties to a less extent than the tubercle bacillus. Several observers have mentioned variation in staining reaction dependent on the nature of culture media or stage of subculturing. For instance, some claim the acid resistance to be greater when the organism is grown on drier culture media, and others claim each successive transfer or subculture shows a gradually decreasing degree of acid-fastness. A. Moeller, though, claims the smegma bacillus to be absolutely acid-alcohol-fast, not decolorized by twelve minutes' application of 3 per cent. HCl-alcohol and not diminished in this property after twenty-five generations.

Possibly the best idea of the various methods is obtainable from a summary and classification used by Drs. Young and Churchman. A brief form of their classification follows:

I. *Methods Depending on Greater Avidity of Smegma Bacillus for the Stain.*

(*a*) Method of Giacomi: Specimen in carbol-fuchsin heated barely to steaming; smegma bacilli deeply stained; Tubercle bacilli not at all or only faintly stained and easily decolorized.

II. *Methods Depending on Decolorization without Alcohol.*

(*a*) Method of Gabbett: Specimen heated in carbol-fuchsin, washed in water, decolorized, and counterstained with Gabbett's solution of methylene-blue, H_2SO_4, and water.

(*b*) Method of Ziehl-Neelsen: Specimen heated in carbol-fuchsin, washed in water, decolorized by H_2SO_4, and counterstained in aqueous methylene-blue.

(*c*) Method of Fränkel: HNO_3 replacing H_2SO_4 in (*a*).

(*d*) Anonymous method (recommended by Alvarez and Tavel): Glacial acetic acid replacing H_2SO_4 in (*a*).

(*e*) Method of Kühne: Carbol-fuchsin to stain, HNO_3 to decolorize, and picric acid to counterstain.

(*f*) Method of Weigert (modification of Gram's method): Stained and treated with KI solution as in Gram's method. Anilin oil to decolorize.

(*g*) Method of Giacomi: Heated in distilled water containing two to three drops of concentrated alcoholic fuchsin, wash in weak solution of perchloride of iron and then decolorize in concentrated solution of the same.

III. *Methods Depending on Decolorization with Alcohol Alone.*

(*a*) Method of Gram: Stain with aqueous solution of gentian violet, then with Gram's solution of KI, decolorize with absolute alcohol.

(*b*) Method of Weichselbaum: Stain in carbol-fuchsin, decolorize, and counterstain with concentrated methylene-blue in absolute alcohol.

(*c*) Method of Czaplewski: Carbol-fuchsin to stain, wash for five minutes in fluorescein methylene-blue, then for one-half to one minute in concentrated methylene-blue.

(*d*) Method of Pappenheim: Stain in carbol-fuchsin, then dip three to five times in solution consisting of absolute alcohol, corallin methylene-blue, and glycerin. Tubercle bacilli are stained red and smegma bacilli blue.

IV. *Methods Depending on Decolorization with Alcohol and Another Agent.*

(*a*) Method of Koch and Ehrlich: Stain for twenty-four hours in anilin water fuchsin (or gentian violet). Transfer to HNO_3, one to four. Place in 60 per cent. alcohol for a few seconds, wash, and counterstain with methylene-blue (or vesuvin).

(*b*) Method of B. Fränkel: Stain with carbol-fuchsin, decolorize with a mixture of HNO_3, alcohol, and methylene-blue.

(*c*) Method of Marzinowski: Stain in watery solution of carbol-fuchsin. Counterstain and decolorize with Löffler's methylene-blue.

(*d*) Method of Lustgarten: Stain twelve to twenty-four hours in concentrated alcoholic solution of gentian violet mixed with aqueous solution of anilin oil. Wash in absolute alcohol, ten seconds in 1.5 per cent. solution of potassium permanganate, then in concentrated aqueous solution of pure sulphurous acid (freshly made by action of H_2SO_4 on metallic copper). After disappearance of precipitate of manganese oxide, repeat permanganate, sulphurous acid, and water until decolorization is complete.

(*e*) Method of Alvarez and Tavel: Same as (*d*) except oxalic acid instead of sulphurous. Also counterstain with saponin, eosin, or picrocarmin.

(*f*) Method of Honsell: Carbol-fuchsin stain, wash, place in acid alcohol (3 per cent. HCl in absolute alcohol) ten minutes, wash, counterstain with alcoholic methylene-blue.

(*g*) Vesuvin and malachite green have also been advised (by Fränkel) and magenta and chyrsoidin (by Gibbs).

V. *Methods Depending on Preliminary Treatment Aimed at Diminishing Resistance to Decolorization.*

(*a*) Method of Matterstock, Bitter, and Markuse: Preliminary solution of fatty substances by ether or chloroform. Stain as usual.

(*b*) Method of Gottstein: Heat specimen with KI in alcohol, wash in alcohol and water; the fatty substances are removed and the specimen is then stained as usual.

(*c*) Method of Bunge and Trautenroth (method for spores): Fix specimen and remove fat by absolute alcohol. Then treat with 5 per cent. chromic acid, stain with carbol-fuchsin, decolorize with dilute H_2SO_4 then with pure HNO_3, counterstain with concentrated alcoholic methylene-blue.

CULTIVATION. Cultivation of the smegma bacillus is one of the most fruitful sources of confusion and difference of opinion among

various workers. Laser, in 1897, claimed to have cultivated it and Czaplewski, a little later, claimed to have secured the first pure cultures. Others followed quickly with similar claims, but more recent workers and the growing consensus of opinion seems to discredit these claims, believing that some other members of the acid-fast group instead of the smegma bacillus were cultivated.

The finding of these men and others who have claimed its cultivation was the result of accident, their purpose usually being to culvitate gonococci or to find a cause of syphilis.

The uncertainty about the reliability of their results is strongly substantiated by both the widely differing results and the ease with which some have obtained growth on almost any kind of culture media, as contrasted with the absolute inability of others to get any growth whatever. A brief summary of their claims, is here given:

The first cultures were made upon agar plates and slants which had been smeared with sterile human blood and incubated twenty-four hours to prove sterility before inoculation. Growth resulted in small colonies like diphtheria or streptococcus. Transplanted to blood-serum and glycerin-agar the growth continued in the same small almost dew drop-like colonies. Most investigators report a difference in cultivation between smegma bacilli and tubercle bacilli in that the smegma bacillus grows more rapidly—a few reporting several days required—but it is usually reported as growing within twenty-four hours to a few days.

The growth on different kinds of media is as follows:

Agar smeared with sterile human blood: numerous, small, diphtheria or streptococcus-like colonies showing mainly micrococci, but after several days are found a few, small, irregularly rounded, grayish-white colonies which prove to contain smegma bacilli.

Gelatin: No development. Some claim slight growth of rather short bacilli, often curved and knotted or with ends swollen in club-like swellings. Weber claims the growth to be composed of quite large bacilli.

Agar slants and plates: Sparse growth after several days at 37° C.

Peptone water and bouillon: Scarcely noticeable growth of a flocculent grayish color.

Glucose bouillon: Marked development in twenty-four hours. White sediment loosened in shreds on shaking. Moeller claims a dry pellicle-like growth floating on the surface of the bouillon, which sinks to the bottom in fragments on shaking.

Potatoes: No visible growth after three days, but rather long bacilli found on scraping the surface for a smear. Later scanty growth, yellowish layer, irregular shape, and indefinite outlines. Weber characterizes the bacillus grown on potato as short and almost coccus-like. He also claims better growth if the potato is alkaline in reaction.

Nutrose-serum agar (used for Czaplewski's first culture): Numerous, small, irregularly rounded colonies of rather long bacilli.

Glycerin agar: Twenty-four hours showed distinctly visible growth, a grayish, well-defined layer. Forty-eight hours showed thick, grayish-white, or yellow growth, margins sharply defined, indented and lobulated appearance, centre darker.

Löffler's serum: Twenty-four hours gave scarcely visible growth. Forty-eight hours, a yellowish-gray color. Variable size from mere specks to areas 2 mm. in diameter, which by confluence later formed a distinct layer. Bacilli often appear granular and as short rods.

Glycerin-milk agar (used and prepared by Neufeld): Claimed to reproduce more nearly the natural conditions of nourishment and to resemble smegma so closely that the bacilli grown on it are more like those observed in direct smear preparations, *i. e.*, some claim that a shorter, plumper bacillus grows on this medium.

Milk medium seems especially likely to produce a growth characterized by an abundance of pleomorphic forms. It is not coagulated, however, by the growth.

Weber reports the successful use of lanolin agar, claiming growth in sixteen out of eighteen cases showing smegma bacilli in one series examined. Stab cultures in agar and gelatin show limited extent of growth which is quite closely confined to the path of the needle. All agree upon an optimum temperature of 37° C.; no growth below 23° C.

The microscopic appearance of a colony of smegma bacilli (especially with the large flat colonies found on glycerin-agar) is wax-like, white or nearly so, dense, finely granular, and with sharply defined margins. The colonies are not always circular, yet never sharply angular, but their irregularities consist of rounded and lobulated extensions. The higher power of the microscope used on a stained impression smear from one of these colonies shows very well the arrangement of the smegma bacilli in the colony, often quite like tubercle bacilli. The bacilli may be in straight lines end to end, as portions of concentric circles, or branching from each other at various angles or forming long parallel lines.

PATHOGENICITY. On one point every investigator presents the same report, and that is the pathogenicity of the smegma bacillus. All agree in saying that it is a harmless, non-pathogenic organism, *i. e.*, a saprophyte. All pieces of work are practically a unit on this, that animal inoculation fails entirely to produce any serious results. Some claim, though, that a slight tubercle-like swelling or nodule is produced at the point of inoculation.

The one case reported by Dietrich of finding smegma bacilli in an ovarian cyst would seem to indicate the possibility at least of the organism possessing some pathogenicity. As mentioned above, the probable explanation of this case is the entrance of the bacilli by digital examination.

It might be added that the unity of opinion on the question of pathogenicity does not seem to verify the claims of cultural findings; for if others than the true smegma bacillus were really cultivated, they were all of the same class, harmless acid-fasts, and hence unable to give positive inoculation results.

PART II.—LABORATORY WORK.

The laboratory side of this paper, undertaken with a view of determining the prevalence of the smegma bacillus about the male genitalia and of verifying some of its cultural and staining properties, must from the nature of the object as thus stated divide itself into two main parts: The first consisted of collecting smegma from which smears were made to be stained and tabulating results of urinary examinations in this laboratory during the past two years. The second consisted in taking swabs or collecting larger amounts of smegma to be used for planting out on several kinds of culture media in an attempt to grow the smegma bacillus.

For this material, access was kindly granted to the male wards of the Wisconsin State Hospital for the Insane and the Dane County Asylum, and to Drs. Lorenz and Stebbins for kindness and coöperation, thanks are gladly extended.

Tabular form[1] will best show the results of each piece of work, preceded by a brief explanation of method or technique used, and followed by summary of results obtained. The first series will consist of a number of cases from which smear preparations were taken, stained, and studied. No complicated plan or procedure was required for this. The inmates were simply taken one at a time, the penis examined for presence of smegma in sufficient quantities for the purpose of this study, and then a number of smears were made on glass slides, banded together and numbered. Or if, as was true in many cases, the smegma found was the product of too long accumulation and therefore too thick and dry to be smeared out at once, a sufficiently large piece was removed and taken to the laboratory to be mixed with sufficient sterile water to make the required number of smear preparations. Then these, together with the rest, were fixed by heat and stained as follows: one in a borax solution of methylene-blue; one in carbol-fuchsin followed by decolorization with 25 per cent. H_2SO_4 until the slide presented the same appearance of decolorization as is usually presented by a slide of sputum stained and decolorized for tubercle bacilli, and then, after examination, counterstained in borax methylene blue (the oil being carefully removed with xylol before counterstaining); one in carbol-fuchsin followed by decolorization with acid alcohol

[1] Detailed tables omitted on account of length.

(5 per cent. HNO_3, 70 per cent. of 95 per cent. alcohol, 25 per cent. H_2O) until the slide presented usual pale appearance; and one in carbol-fuchsin, followed by decolorization with Labarraque's solution until the slide had assumed a distinct brown color.

All carbol-fuchsin staining was done with Ziehl's carbol-fuchsin for twleve hours in a paraffin oven at 50° C. or twenty-four to thirty-six hours at room temperature.

No. of cases.	Stain.	Decolorizer.	Counterstain.	No. showing smegma bacilli.	No. not showing smegma bacilli.
126	Carbol-fuchsin	H_2SO_4	None	85	41
112	Carbol-fuchsin	H_2SO_4	Methylene-blue	19	107
196	Carbol-fuchsin	Acid alcohol	None	16	103
117	Carbol-fuchsin	Labarraque's solution	None	16	101

SUMMARY OF TABLE. Of 127 cases taken, practically all present the same picture when stained with methylene-blue. A number of different kinds of cocci and bacilli are present in abundance, the predominating organism always being mentioned first. Many of the bacilli are diphtheroid in appearance. The chief difference between any one slide and another is simply a matter of degree and proportion of each kind of organism, each having the same types.

Of 126 stained with carbol-fuchsin and decolorized with 25 per cent. H_2SO_4, 41 cases, or 32.5 per cent., failed to show any red bacilli at all, while 85 cases, or 67.5 per cent. showed red bacilli in greater or less abundance as described under each case as to size, shape, etc.

Of the same 126 cases counterstained with methylene-blue, 85 of which had shown red bacilli before counterstaining, only 19 cases, or 22 per cent., continued to show them in greater or less numbers, *i. e.*, 77 per cent. of the cases showing red bacilli before counterstaining lost or had their red stain masked when counterstained.

Of 119 cases stained with carbol-fuchsin and decolorized with acid alcohol, 16 cases, or 13 per cent., showed a few or more red bacilli, usually very faint red or in larger masses of debris in the preparation which had not been so thoroughly subjected to the action of the decolorizer.

Of 117 cases stained with carbol-fuchsin and decolorized with Labarraque's solution, 16 cases, or 13 per cent., showed red bacilli in varying numbers and in varying stages of decolorization from faint red almost decolorized to dark red bacilli, as yet unmodified by the action of the decolorizer.

Since the material in the above series was secured from a class of men whose condition would mean habits of cleanliness not up to the average standard, a series of 20 cases from normal men was studied, somewhat as a control for results of the first series. The

subjects from whom these specimens were obtained were men about the laboratory, faculty, and students.

Material was collected as for the first series, save that only H_2SO_4 was used as a decolorizer, the purpose being merely to determine the presence or absence of smegma bacilli.

Of 20 cases studied in this second series, 13, or 65 per cent., showed the presence of smegma bacilli when stained with carbol-fuchsin and decolorized by 25 per cent. H_2SO_4. This is to be compared with 67.5 per cent. in the first series.

Two cases, or 10 per cent. of all cases, still continued to show smegma bacilli even after counterstaining. This corresponds to 14 per cent. similarly obtained in the first series.

Methylene-blue used alone showed the same results as in the first series.

URINE. From an interest in the findings and conclusions of Young and Churchman that urine could not be safely collected unless by their method, which provides for previous urethral irrigation, and the conflicting statement of other writers that catheterization is sufficient, a study of the case records of this the State Laboratory of Hygiene has been made. This covers a period of the past two years, and includes all the cases of urine examined for tubercle bacilli, whether this examination was especially requested and indicated by history and suspicions of genito-urinary tuberculosis or was simply made as a part of the routine examination of urine.

The results of this study are tabulated below:

Findings.	To be examined for tubercle bacilli.	Routine examination.
Positive to tubercle bacilli	3	2
Negative to tubercle bacilli	10	18

This shows 22.5 per cent. of cases of suspected tuberculosis to show acid-fasts and 10 per cent. of cases not suspected, or 14 per cent. of all cases examined for tubercle bacilli. These cases are taken as they came into the laboratory from all over the State, without special precaution or technique to avoid getting smegma bacilli into the urine, and probably few were collected by catheter.

Young and Churchman report 11 cases out of 24 collected similarly as positive, or 45 per cent., as compared with 14 per cent. found here, including more than one-third of the cases in which diagnoses of genito-urinary tuberculosis had already been made or suspected. This would tend to show less chance of the smegma bacilli getting into the urine than these workers suggest.

CULTIVATION. *Technique.* The second portion of the laboratory side of this study consists of a series of cultures from 42 cases, taken in different ways, treated differently, planted differently, and incubated differently in an effort to produce growth.

The material for the first 32 of these was collected from the penis by the usual sterile swab used for the taking of cultures and planted on various kinds of artificial culture media—meat-lactose-agar, human hemoglobin-agar, cat-blood agar, blood-serum, meat plain agar, and meat-glucose-agar. Cultures were incubated at 37° C. aërobically or anaërobically, as the case might be, until examined. Examination of smear preparations was made after varying periods of two days to two weeks, and with two staining methods. One preparation was stained with borax methylene-blue and the other with carbol-fuchsin, followed by 25 per cent. H_2SO_4 to decolorize, then examined, counter-stained with methylene-blue, and again examined.

The technique for the last ten cultures differed slightly from the first series. The antiformin method for isolation of tubercle bacilli was used on large quantities of smegma taken from several of the more abundant cases and the sediment planted out on Dorset's egg medium, three or four loopfuls each to the first two tubes and the remainder poured into the third.

Results. Of the 42 cases studied, the first 32, or those planted as from ordinary swabbing, show but little difference save the 6 grown anaërobically, and these seemed to have slightly less abundant growths. In all cases, however, the growth was quite abundant, and upon examination proved to contain the same organisms, cocci and bacilli, of several kinds and in varying proportions. Very often bacilli were found which were so like diphtheria bacilli that a differentiation could be made only with difficulty, if at all. Many others, while not resembling the diphtheria bacillus so closely as to be called pseudodiphtheria, still were enough like to to be called diphtheroid. These are probably the same organisms mentioned by several observers in their writings on the smegma bacillus.

Stained for acid-fasts, these same preparations failed to show any organisms which had resisted decolorization, only a few doubtful ones being found, and these were quickly proved negative on counterstaining.

The last 10 cases treated by a method calculated to eliminate the abundant growth of other bacilli and cocci failed to show any better results, save that the growth was less abundant.

Conclusions. From the foregoing we can see several conclusions quite clearly set forth for us, not least among which is the need for a thorough, comprehensive, dependable piece of work on this subject.

From the knowledge at hand it is evident that:

1. The smegma bacillus resembles the tubercle bacillus very closely in staining properties and in morphology.

2. No method of differentiation by staining is entirely adequate for all cases.

3. The successful cultivation of the true smegma bacillus is open to question.

4. Successful cultivation granted, the inherent difficulties by methods now available render this method of differentiation of little value in routine diagnosis.

5. The smegma bacillus is found in a large proportion of patients examined, but the widespread occurrence is quite dependent on the degree of cleanliness of the patient, together with the presence or length of foreskin in males.

6. By thorough cleaning of the genitalia, especially the meatus and by catheterization, urine to be examined for tubercle bacilli can be collected with a fair degree of certainty of freedom from smegma bacilli.

7. With the above precautions, the finding of acid-fast organisms after decolorization with acid-alcohol enables us to make a presumptive diagnosis of genito-urinary tuberculosis.

8. Final differentiation, however, can be made only by animal inoculation.

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REVIEWS

INFECTIONS OF THE HAND. A GUIDE TO THE SURGICAL TREATMENT OF ACUTE AND CHRONIC SUPPURATIVE PROCESSES IN THE FINGERS, HAND AND FOREARM. By ALLEN B. KANAVEL, M.D., Assistant Professor of Surgery, Northwestern University Medical School, Chicago. Second edition; 463 pages; 147 illustrations. Philadelphia and New York: Lea & Febiger, 1914.

AFTER disposing of simple localized infections, as paronychia, carbuncle, etc., in Part I, the remainder of the book discusses the grave infections as tenosynovitis, fascial-space abscesses, lymphangitis, and their sequelæ from the anatomical and clinical stand-points. The tendon sheaths of the fingers with their communications and the extensions into the radial and unlar bursæ are described. Five well-defined fascial spaces are exposed: the middle palmar, the thenar, the hypothenar, the dorsal subcutaneous, and the dorsal subaponeurotic. The relation between the tendon sheaths and the palmar spaces is considered. About this outline revolves the theme of the whole book.

The faults of the work are insignificant as compared to its merits. Of the former the chief ones are repetition and lack of a careful finish from the stand-point of uniformity of nomenclature and expert proof-reading. Chapter XV, which gives excerpts from the literature, might well be omitted. It consists of literal translations from French and German authors. It is difficult to understand why English and American authors are entirely neglected. By better arrangement of its contents and avoidance of repetition, as for example the description of the treatment of infections once instead of several times, the bulk of the book could be advantageously reduced. Several omissions and statements occur to which we believe exception may be taken. For example, a noteworthy omission is the differential diagnosis between traumatic neuritis from direct trauma to the nerve (usually the median) in a punctured wound and actual infection of the hand. The author "condemns most severely" the excision of a carbuncle. In cases of grave septicemia from this cause it appears to be just as rational *immediately* to prevent further absorption of toxins by excision of a carbuncle with cauterization of its base as it is

to amputate a putrid limb under similar conditions. We are not aware that streptococci produce pus, but we do know that they are frequently forerunners of the pyogenic staphylococci. While we agree that isolated necrosis of a metacarpal is commonly tuberculous, we disagree as to its frequency in syphilis, since in our experience the latter disease produces a characteristic *proliferative osteoperiostitis*. The sentence: " . . . temperature running a classical hectic curve (98° to 102° F.), then constantly between 120° and 130°, having the appearance of impending death" possesses a little ghastly humor. Blood-counts are not usually estimated in centimeters but in millimeters.

The masters Tillaux, Malgaigne, and Cannon are named Tilleau, Tilleaux, Malgaine, and Canon respectively. The references to some of the figures are wrong and sometimes leaders and legends are missing. It would facilitate references to mention the pages on which the figures appear.

The value of the monograph cannot be overestimated. After carefully reading it there is no excuse for the operator who does not immediately get better results with his cases of infected hands. So far as the wage-earner is concerned a restoration to complete function in 95 per cent. of the abscesses of the fascial spaces and the reduction of the morbidity in tendon-sheath infections by one-half are matters of superlative economic importance. It may readily be seen that the message the book carries must eventually promote the weal and welfare of humanity. P. G. S., Jr.

Clinical Diagnosis. By Charles E. Simon, B.S., M.D., Professor of Clinical Pathology and Experimental Medicine, College of Physicians and Surgeons, Baltimore. Pp. 809; 210 illustrations. Eighth edition. Philadelphia and New York: Lea and Febiger, 1914.

It is fortunate indeed that such an early demand for a new edition of Simon's *Diagnosis* should have arisen. It has given the author an opportunity to introduce a wealth of new material, the product of the last two years, as well as to carefully revise the old.

The quantity and quality of the new material is of special interest and brings one up to the minute in laboratory diagnostic technique. It includes a concise and lucid account of the diagnostic methods dependent on the appearance of the protective ferments of Abderhalden in the blood and opens the gates to this new and attractive field of "organ diagnosis."

The Wassermann reaction has received a thorough rewriting.

with special emphasis on the desirability of uniformity in the various reagents, notably the antigen. The compliment-fixation test in latent gonococcus infections has been included in this edition.

In the discussion of the functional tests of the kidney the author declares himself for the phenolsulphonephthalein test and wisely confines himself to a description of this test alone. He shows that its use is practicable and urges its adoption by the general practitioner.

The division of the book into two sections, the first dealing mainly with technique and the second with the application of this information in concrete diseases, is continued in this edition. This description of the correct interpretation of laboratory data, under varying clinical conditions, is invaluable and will appeal especially to those who are depending on others for their laboratory work.

The present arrangement of the book, the character as well as the happy presentation of the information it contains, assures its continuance in the forefront of works of its kind. A. A. H.

MEDICAL GYNECOLOGY. By S. WYLLIS BANDLER, M.D., Adjunct Professor of Diseases of Women, New York Post-Graduate Medical School and Hospital. Third edition; pp. 790; 150 illustrations. Philadelphia and London: W. B. Saunders Company, 1914.

THE practical value of a book of this nature is attested by the appearance of a third edition. A thorough revision has included the more important advances of the five years which have elapsed since the second edition was published. The most extensive revision occurs in the chapter on internal secretions, where the author details our present knowledge of the relationship between the glands of internal secretion and the genital tract of women, and refers to the merits of organotherapy. The broader aspects of certain cases are set forth in a notable chapter on the associated nervous conditions in gynecology. Mention must also be made, especially as regards the sections on treatment, of the chapters dealing with constipation, the anomalies of menstruation, and gonorrheal infections. The author considers it as essential that the public be educated concerning the early symptoms of carcinoma.

As a very complete and effective presentation of practical non-operative measures in gynecology the book will be of much service to all engaged in this branch of medicine. P. F. W.

THERAPEUSIS OF INTERNAL DISEASES. Edited by FREDERICK FORCHHEIMER, M.D., Sc.D. (Harv.), Professor of Medicine, Medical Department, University of Cincinnati (Ohio-Miami Medical College). Four volumes and a desk index. Vol. I, pp. 795; 67 illustrations. Vol. II, pp. 874; 35 illustrations. Vol. III, pp. 984; 41 illustrations. Vol. IV, pp. 942; 45 illustrations. New York and London: D. Appleton and Company, 1913.

DURING the past five years several admirable systems of therapeutics have been published in this country. The last and most comprehensive of these works to appear is *Therapeusis of Internal Diseases*, edited by Frederick Forchheimer. Although this work embraces four volumes, none of the volumes contains more than a little over nine hundred pages, and their size prevents them from being in any sense cumbersome. The addition of a desk index in a small separate volume adds materially to the convenience and ease with which the books can be used.

As must be the case in so extensive a work, the various subjects, which include practically the whole realm of internal medicine, are discussed by a large number of different authorities. Here the word "authorities" may with propriety be used in its literal sense, for a survey of the list of collaborators discloses the fact that in nearly every instance those selected to contribute to these volumes have been eminently qualified for the tasks assigned them. In spite of the diversity of subjects discussed by such a number of different authors a surprising degree of uniformity has been obtained, a fact which implies that the entire work has been subjected to exceedingly careful editorial supervision. Indeed, throughout all the volumes, especially when differences of opinion exist, pertinent editorial notes and comments abound.

The first volume is devoted to the fundamental principles of general therapy, and consists of a group of noteworthy contributions which furnish a firm and sound foundation for the special therapeutic considerations which are contained in the other volumes. All the chapters in this volume are of importance and interest, but among those which are conspicuous may be mentioned that on organotherapeutics by Reid Hunt, Francis Carter Wood's admirable discussion of vaccines and serum therapy, climatology by Henry Sewall, and the contributions of Warren Coleman on nutrition and dietetics, and of Victor C. Vaughan on toxicology. Hydrotherapy, exercise, and various forms of mechanotherapy, as well as radium and the *x*-rays and psychotherapy, are all given careful consideration.

In the remaining three volumes special therapy is taken up. This comprises a detailed discussion of the treatment of all the diseases included under internal medicine. Volume II deals with

the treatment of the acute infections, the intoxications, and constitutional diseases. One of the most complete contributions under the infections is Frederick C. Shattuck's discussion of typhoid fever, in which he advocates a liberal dietary, although he belittles the necessity of basing such a diet upon definite caloric values. Henry L. Elsner has written an excellent article on the treatment of pneumonia, in which he takes a decided stand in favor of the open-air treatment of this disease. Gottheil's article on syphilis is also worthy of note, as are the contributions of John Ruhräh on smallpox and vaccination. Under the intoxications are discussed alcoholism, opium, phosphorus, food poisoning, pellagra, and intestinal auto-intoxication. The section on constitutional diseases is wholly excellent, as might be expected when the contributors of these chapters are considered. Charles Lyman Greene writes on the difficult subjects of myositis, gout, and arthritis deformans. Davis Riesman's consideration of diabetes mellitus and diabetes insipidus is admirable, and obesity and rachitis are well handled by Edwin A. Locke and Isaac A. Abt respectively.

Volume III begins with diseases of the digestive tract. Of the numerous excellent articles that come under this heading none are more valuable than Louis Starr's timely discussion of diseases of the mouth, and Wilder Tileston's chapter on pancreatic disease. Diseases of the respiratory tract are next considered by such able writers as B. R. Shurly, Robert D. Rudolf, Allison Walter Hewett, George Blumer, and Joseph C. Capps, whose contributions leave nothing to be desired. The third section of this volume is devoted to diseases of the circulatory system. Pericarditis is considered by Alexander and William F. McPhedran, while all other circulatory diseases are taken up by Charles Spencer Williamson. The final section is given over to diseases of the blood and ductless glands. All the chapters on blood diseases are written by C. F. Martin, and Frederick Forchheimer, the editor, contributes the carefully prepared chapters on diseases of the adrenals, the spleen, and the thyroid and parathyroid glands.

In the last volume, Volume IV, diseases of the kidneys, diseases of the bladder, gonorrhea, and other diseases of the male sexual organs, nervous diseases, and diseases due to protozoa and the various tropical diseases are all considered. The management of nephritis and amyloid disease of the kidney is discussed by Joseph L. Miller, while the treatment of other kidney conditions has been left to the facile pen of Frank Sherman Meara. Genito-urinary conditions are well discussed by E. L. Keyes, Jr. Organic diseases of the nervous system have been written by Joseph Collins, Edwin G. Zabriskie, Howell T. Pershung, and John Grinker, while the neuroses are taken up by Lewellys F. Barker and Smith Ely Jelliffe. The various phases of tropical diseases are carefully considered by such well-qualified observers as William B. Wherry, Paul G. Woolley, and Creighton Wellman.

It is obvious that to attempt to discuss critically the vast and varied field covered by these volumes is well-nigh out of the question. The above brief sketch of their contents will at least convey some idea of the thoroughness with which the treatment of internal diseases has been covered and the eminence of the authors to whom this task has been intrusted. In all the contributions certain features are characteristic. The treatment of the various diseases is considered from all aspects, the practical bearing of anatomy, physiology, pathology, and chemistry on the management of diseased conditions is never lost sight of, the various forms of treatment are described in such detail that they may be easily carried out, and unusual emphasis is placed upon the newer forms of specific, hygienic, and mechanical methods of managing disease. The list of important references to the literature given at the end of most of the chapters is a valuable aid to all who may be interested from time to time in the investigation of certain of the subjects.

Too much praise cannot be bestowed upon the painstaking way in which all the volumes have been edited. As a result, they will stand not only as models of valuable works of reference, but what is even more desirable, they are destined to take a prominent place as useful books for the daily help of the practitioner.

G. M. P.

A Text-book of Histology. Arranged upon an Embryological Basis. By Dr. Frederic T. Lewis, Assistant Professor of Embryology at Harvard Medical School, and Dr. Philip Stöhr, formerly Professor of Anatomy at the University of Würzburg. Second edition; 539 pages; 495 illustrations. Philadelphia: P. Blakiston's Son & Co., 1914.

In this revised edition of Lewis' arrangement of Stöhr's *Histology*, over one-fifth of the illustrations are of an embryological character, and the book, as a whole, conforms in a high degree to the plan originally laid down by Professor Lewis. This plan was to present the development of each organ, or system of organs, before detailing the microscopic structure. That this is a valuable addition for a student of anatomy may be seen by examining the introduction to the study of the heart, digestive tube, or reproductive organs. Here are given in short form, with illustrations, a clear account of the changes which occur from the simple form of early embryonic life to the later definitive stages.

An important change from the previous edition is the insertion of references to original sources, not only to recent papers, but also to those authors who first gave a good account of the structures under discussion. Thus we have citations from Robert

Hooke (1664) on cells; Leeuwenhoek (1677) on spermatozoa; Vesalius (1604) on bloodvessels; Aselli (1622) on lymphatics, and many others. These are not given in lists at the ends of chapters, or as footnotes, but are worked into the text in an interesting and attractive way. The result is a stimulating book, which will serve not only to give information, but also to give the student a perspective of his subject, and to teach the discerning ones how to supplement their knowledge by further study. W. H. F. A.

THE BIOLOGY OF THE BLOOD CELLS. By O. C. GRUNER, M.D. (Lond.), Assistant Professor of Pathology, McGill University, Montreal. Pp. 392; 7 colored plates; 75 illustrations. New York: William Wood & Co., 1914.

THIS volume represents an extremely ambitious and complete collection of all the important hematological work that has appeared in the recent literature of the subject. The author has gathered together the various expositions of theories and demonstrations of facts that are in any way connected with the biology of the blood cells and placed them in a form that is readily accessible to those willing to delve into the complicated depth of the morphology, the genesis, the life history, and the functions of the various types of blood cells. It cannot be gainsaid that all this represents a tremendous amount of work; there are 644 separate and distinct references, but the value of such work, representing for the greater part a collection of literature, is certainly open to question. Whether or not such compilations are deserving of particular praise, aside from that which should be given to mechanical perfection of any kind, is very dubious.

The book consists of seven chapters, dealing respectively with primordial, red, lymphocytic, monocytic, neutrophilic, and phlogocytic forms of blood cells, and with the cytoplastic phenomena of blood-forming tissues. Following this there is an appendix containing a list of the abbreviations employed, the references to the literature, and an extremely comprehensive glossary of hematological terms. Last of all are the indices, four in number, a general index, and indices of the diseases, the animals, and the authors referred to.

In reading the book several facts stand out with particular prominence. One is impressed by the intense admiration the author apparently feels for Pappenheim, as shown by the stress he lays upon his theories and ideas, frequently neglecting entirely the opinions of other hematologists, only somewhat less distinguished. One is also impressed by the utter futility of endeavoring

to use the work "as a companion to any of the larger text-books on hematology." The information is so abstruse and so complicated that it would require either a careful study of the book from the beginning to fully comprehend much that is written or else one would have to be a student of advanced hematology to follow the various statements and arguments.

Several criticisms more specific might be made. The author accepts the intermediate view of Pappenheim as to the origin of the blood cells, and seems to dismiss the pure dualistic theory without sufficient consideration. On page 66 no mention is made of the strong possibility of the neuclear body seen in human erythrocytes being an artefact. At times there is a tendency to contradict statements previously made, as with chlorosis and punctate basophilia on pages 79 and 81. Reading page 100, one receives a shock to find that "the ordinary blood-count is of relatively small value in elucidating the pathology of a case of anemia." On page 167 reference is made to Asher's work upon iron metabolism and the spleen, but the iron content of the feces was estimated, not that of the urine. Similar minor errors, for the most part unavoidable, are found from time to time in the latter pages. In considering the glossary of hematological terms exception might well be taken to even noticing some of the etymological monstrosities that the author has seen fit to include for the sake of completeness. Incidentally he here tabulates 86 synonyms for Pappenheim's lymphoidocyte.

The necessity of such a book as the present one may be questioned; there can be no question but that the subject matter is presented in a deeply scientific and scholarly fashion. The author has done well a difficult and imposing task. J. H. M., Jr.

Massage, Manual Treatment, Remedial Movements, History, Mode of Applications, and Effects; Indications and Contra-indications. By Douglas Graham, M.D., Consultant and Instructor in Massage, Boston, Massachusetts. With a Chapter on Massage of the Eye, by Dr. A. Darier, formerly President of the Ophthalmological Society of Paris; Chevalier of the Legion of Honor, etc. Fourth edition; pp. 574; 75 illustrations. Philadelphia and London: J. B. Lippincott Company, 1913.

This the fourth edition of "the first book on massage in point of time in the English language" appears as a well-bound, splendidly printed volume.

The revision has not been extensive, and certainly seems to fall

short of the possibilities of such a work eleven years after the appearance of its admirable predecessor. Twelve new illustrations, about forty paragraphs, and a chapter on massage of the eye constitute the additions. A few paragraphs have been omitted. The new paragraphs usually introduce or conclude the chapter as it appeared in the former edition, and touch upon the possibilities of massage in such conditions as angina pectoris, arteriosclerosis, atonic dilatation of the stomach, pneumonia, etc. Some few lines are devoted to Bier's hyperemia.

The author still feels that manipulation of the gall-bladder through the abdominal wall may aid in the solution of biliary calculi, and he seems to have little respect for the surgeon's viewpoint of appendicitis.

The book remains largely a record of the early personal experiences of a man who is intensely enthusiastic about his subject, but has allowed himself to be slightly overbalanced by it.

The chapter dealing with the mode of applying massage is excellent. The illustrations are very good. As a new edition it is somewhat of a disappointment; as a book on massage it remains an excellent treatise. T. G. S.

Modern Radium and Thorium Therapy in the Treatment of Tumors, Gout, Rheumatic Diseases, Neuralgias, and the Diseases of the Blood. By Adolph Bickel, M.D., Professor in the University of Berlin. Pp. 40. Berlin: August Hirschwald, 1914.

This is a small monograph on the treatment of various conditions by radium and mesothorium. The author reviews briefly the physics of radio-active substances and radio-activity, the indications for the use of the two mentioned and their value, and gives a summary of cases he has treated. H. K. P.

Modern Surgery. By John Chalmers DaCosta, M.D., LL.D., Professor Surgery, Jefferson Medical College, Philadelphia; Surgeon to Jefferson Medical College Hospital; Surgeon to St. Joseph's Hospital; Fellow of the American Surgical Society, etc. Seventh edition; Pp. 1515; 1085 illustrations. Philadelphia and London: W. B. Saunders Company, 1914.

This the seventh edition of the author's work has added much to his already valuable treatise on surgery. The book has been reset, and to keep the work in as small a compass as possible the

pages were made longer and wider, thus keeping the bulkiness at a minimum. An endeavor has been made to steer a mid-course between prolixity and brevity, to winnow the grain from the chaff of all that has been published in recent years as truths, and by giving opposing views, in some instances to allow the reader to choose.

Due credit is given every author for his work, and in many instances the original author's own description is quoted *verbatim*. Many statements of discoveries or findings are accompanied by the author's name and reference to the article, thus enabling easy reference to the original if so desired.

The subject has been brought as nearly up to the day as any work can be in this age of such rapid strides in surgery and its allied subjects. The chapters on laryngology are very good, containing the very latest and approved literature on tracheobronchoscopy and esophagoscopy.

The chapters on bacteriology, seriology, and radiography are well presented, and make very clear, instructive, and interesting reading.

The entire subject of surgery is well covered, in fact as completely as can be done in a one-volume book, although the reviewer ventures to suggest that more text space could have been used for descriptions of operations such as are seldom found outside an operative surgery. This space could have been obtained by omitting some of the illustrations of bacteriological slides, monstrous tumor specimens in the late stages, when a diagnosis is either useless or certain, or both.

Careful reading found several minor failings, such as an instance of faulty indexing, which is merely incorrect page quotation, one or two of the fracture dressings differ rather widely from the general use, but this is a matter of personal opinion and adaptability to individual cases.

On the whole the book is an excellent one, well illustrated, and up to date. It makes pleasant, easy, and very instructive reading. The vocabulary and style are typical of the author—excellent.

The work may well grace the shelf of either a surgeon or a student still in his undergraduate course. E. L. E.

CLINICAL DISORDERS OF THE HEART-BEAT. By THOMAS LEWIS, M.D., F.R.C.P., Assistant Physician and Lecturer on Cardiac Pathology, University College Hospital. Second edition, pp. 116. London: Shaw & Sons, 1913.

THE prompt appearance of a second edition of this little book attests its popularity among medical men. This new edition

in no way differs from the earlier one except for the addition of a chapter upon auricular flutter. The author describes the nature of this rare cardiac disorder, discusses its etiological and pathological relations, details its symptomatology and mode of recognition, and outlines the course of treatment. The incorporation of this chapter brings the book fully up to the present-day knowledge of cardiac arrhythmias, making the book of great value to those sufficiently interested to desire a clear working knowledge of this interesting phase of disturbances of the heart.

J. H. M., JR.

A MANUAL OF ELEMENTARY ZOÖLOGY. By L. A. BORRADAILE, Lecturer in Zoölogy, University of Cambridge. Pp. 470; 301 illustrations. London: Henry Frowde, Oxford University Press.

THIS book, as the title indicates, is one of that large class of texts which aims to present the main facts of zoölogy without making any attempt to outline a method of teaching the subject. It departs somewhat from the exact type of manual indicated by devoting the first 108 pages to a detailed consideration of the frog. Following this the larger groups of animals are taken up in the order of their complexity and considered in much less detail. It is the apparent purpose of the author to give the main facts concerning the group, and this is done sometimes by the discussion of a single animal and sometimes of several. As a rule a single chapter is devoted to a Phylum but in some cases such material is distributed through a number of chapters. The Porifera, Echinodermata, the worms aside from the Annelida, and Reptilia are omitted. General subjects under the headings "Reproduction and Sex," "Embryology," "Classification and Evolution," "The Animal and the World" are discussed in separate chapters. The illustrations are numerous and generally good. Marginal references in bold faced type and italicized terms in the text are commendable features of a uniformly good typography.

There does not appear to be any good reason in the nature of this book why it should be added to the already overcrowded market. No conspicuous merit of subject matter or method characterizes it, while on the other hand there is a lack of balance, and not a little misinformation to be found. A better acquaintance with researches in countries other than his own would have served to keep the author from many mistakes. Indeed, the book is distinctively English throughout and has the strength as well as the weakness which characterizes the biological writings from that country. It will probably make its own individual appeal and find a place of usefulness, and if there is to be a multiplicity of books of one kind it has quite as much right to exist as many others.

C. E. M.

TREATMENT AFTER OPERATION. By WILLIAM TURNER, M.S., F.R.C.S., Senior Surgeon to the "Dreadnought" Seaman's Hospital Greenwich, etc., and E. ROCK CARLING, B.S., F.R.C.S., Surgeon to the "Dreadnought" Seaman's Hospital Greenwich, etc. Containing a chapter on the Eyes, by L. V. CARGILE, F.R.C.S., Senior Ophthalmic Surgeon and Lecturer on Ophthalmology, King's College Hospital, etc. Pp. 247; 55 illustrations. London: University of London Press.

As is indicated in its preface this work is especially valuable, to house surgeons, students, and nurses. The data is obtained entirely from the personal experience of the writers and no attempt has been made to elaborate theories or modifications of treatment.

The treatment is begun in the sickroom before operation and the patients followed through their convalescence, each symptom and sign demanding treatment being taken up and disposed of. In many minor points, the procedures used are not altogether approved by surgeons at large. Cracked ice for thirst is an atrocious practice. Drugs for postoperative vomiting are useless. More stress should be laid on the stomach tube.

Many of the illustrations are exceedingly well chosen, but several leave much to be desired in what they are intended to show.

In conclusion, I would commend the book as a fairly complete *resume* of after-treatment which will be of wonderful aid to surgeons of little experience as the authors state. E. L. E.

THE PEOPLE'S MEDICAL GUIDE. By JOHN GRIMSHAW, M.D., B.S. (Lond.), D.P.N. (Camb.), M.R.C.S. (Eng.), etc. Pp. 839; 112 illustrations. New York: Macmillan Co.

IN scope this book is a veritable medical encyclopedia of such information as should be at the disposal of the public.

The sections devoted to the dietetics and hygiene of infancy and childhood are excellent in every way; their true import is lost, however, unless their relationship to the normal development of teeth, digestive tract, bones, and nervous system is appreciated. The author contends that a normal adult is an impossibility unless preceded by a normal child, and that a normal child is likewise impossible unless nature's laws are understood and followed. The onus of the situation thus falls on the parent and doctor to keep rather than get the child well.

Under infectious and contagious diseases the interests of the community were kept well to the fore. The public conscience is sharply prodded as regards reporting and quarantine as well as

regarding measures preventive to the spread of disease not generally considered as contagious.

The portion devoted to surgical conditions should dispel much of the present ignorance and dread of surgical procedures as such and should leave clearly in mind set conditions in which surgery holds the only hope of recovery.

Such broad questions as eugenics, venereal disease, and cancer are thoroughly discussed.

Much valuable material is found in the final sections on feeding and exercise. Not only are these of interest as applicable in diseased states but also in the daily business of keeping a healthy body well.

The author, in so far as the main object of his book is concerned, seems to have somewhat overshot the mark. His subtitle reads in part, "Points for the Patient, Notes for the Nurse, Matter for the Doctor." That these three types of information are found is true. To the doctor and nurse this will not prove confusing, but a patient might, at times, trespass on forbidden ground to his sorrow. A. A. H.

THE MOSQUITO: ITS RELATION TO DISEASE AND ITS EXTERMINATION. ALVAH H. DOTY, M.D., formerly Health Officer of the Port of New York. Pp. 79; 10 illustrations. New York and London: D. Appleton & Company.

THIS little book, from the pen of one who is so well qualified to speak with authority on this subject, will find many readers. Simplicity and clearness, both in the text and illustrations form its keynote. This is especially fortunate as the problem of the mosquito, as the author insists, is one which can only be successfully approached by the united effort of all. A working knowledge is here obtainable presented in such a way as to be above the head of practically no one. A. A. H.

THE DISEASES OF THE SKIN. By WILMOT EVANS, M.D., B.S., B.Sc., F.R.C.S., Surgeon to the Royal Free Hospital, and Surgeon to the Skin Department, Royal Free Hospital; Senior Surgeon to the Hospital for Diseases of the Skin, Black Friars. Pp. 375; 32 illustrations. London: University of London Press.

THE author of this small volume which is intended as an introduction to the study of diseases of the skin, has succeeded remarkably well in the always difficult task of combining clearness of

description with great conciseness. While it is, of course, impossible to discuss with any degree of detail the various diseases of the skin within the limits of such a manual, yet the essentials of the subject are well covered. The author's views are in the main those commonly held, but in a few instances they are somewhat at variance with usually accepted ones. Ecthyma is regarded as simply a variety of impetigo contagiosa, an opinion which scarcely seems to be in accord with clinical facts. Herpes labialis, especially that variety associated with other diseases, is thought to be due to the organism causing the affection with which it is associated; *e. g.*, the herpes of pneumonia is looked upon as the direct effect of the pneumococcus upon the mucous membrane of the lip, the author having found, as he believes, this organism in the vesicles. Vitiligo is thought to be probably the result of some toxin having its origin in the alimentary canal.

We learn with some surprise that the primrose (Primula obconica) is the most frequent cause of plant dermatitis in England.

The book is a very good one of its class, and will be found useful by the student, but it cannot, and is not intended to, take the place of larger and more formal treatises on diseases of the skin.

M. B. H.

PROMPT AID TO THE INJURED. By ALVAH H. DOTY, M.D., Late Health Officer of the Port of New York. Fifth edition. Pp. 229; 85 illustrations. New York and London: D. Appleton & Company.

THIS book, meeting, as it has in the past, the broad need of a guide in accidents of all kinds, has become more than ever valuable since this latest edition has been brought abreast of the latest knowledge in surgery, medicine, and sanitation.

While its possession will come amiss to no one, its greatest field of usefulness will be found, as of old, where the community masses itself in factories, camps, and similar places; that is, where accidents most frequently occur.

A. A. H.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Wassermann Reaction and its Application to Neurology.—FILDES and MCINTOSH (*Brain*, xxxvi, part ii, 193), maintaining that the mere report of a Wassermann reaction is of little value unless one knows the technique used in securing it, describe at some length the methods employed by them in the study of many neurological conditions. It is interesting that, as a result of careful studies, they have come to use, as an antigen, a cholesterinized alcoholic extract of fresh human heart. The advantages claimed are the great invariability of such antigens, and the fact that they give a much higher percentage of results in undoubted lues, while at the same time they manifest no tendency toward non-specificity findings quite in accord with those reported by Walker and Smith, Kolmer and others. They find that inactivation of sera causes a reduction in the amount of the reacting substances much greater than that observed in inactivated spinal fluids. The preliminary titrations, and dilutions are clearly explained. Their findings in the various stages of syphilis in general accord with those already reported: these in brief are: (1) The reaction is negative in non-syphilitic diseases of the central nervous system. (2) The occurrence of a positive reaction in the spinal fluid is indisputable evidence of a luetic infection. (3) The reaction in cerebrospinal lues varies much according to the location of the process, being inconstant, weak, or negative except when the spinal cord itself is involved, in which case the reaction is remarkedly strong. Moreover in this group of cases they find position reaction more often in cases showing recent lesions. (4) In general paresis a strong reaction is nearly always present in both serum and spinal fluid, the same being true of tabes

unless examined after the disease has existed for some time or has been well treated. (5) So common is the occurrence of a positive reaction in the spinal fluid and a negative one in the serum, and *vice versa*, that the negative finding of one alone is insufficient evidence to exclude a luetic process. As regards the results of specific therapy the authors call particular attention to the fact that some cases of paresis and tabes should not be grouped as "true parasyphilitics," since some are really active cases of lues. They find indeed that the best therapeutic results are secured in those cases in which there is evidence of active meningeal involvement, cases which they regard as transition forms between true dementia paralytica and cerebrospinal syphilis. Treatment has little or no effect upon the Wassermann reaction in pure parasyphilitic cases, a result so different from that seen in cerebrospinal lues as to be of real value in a prognostic sense. It would seem that the rapidity with which a positive spinal fluid can be reduced to a negative state bears little relation to the duration of the infection; this is the reverse in the serum in which the chronicity of the disease varies directly with the speed of change of the reaction. The authors are of the opinion that the "salvarsan-provocative test" has been given an exaggerated diagnostic value.

The Pathological Excretion of Amino-acids.—Lobbe and Bith (*Arch. des malad. de Pappar. dig. et de la nutrit.*, vii, p. 681 to 688), have used a method modified from that of Jäger, in which 40 c.c. of urine are mixed with 10 c.c. of 5 per cent. magnesium hydrate and a few drops of phenolphthalein. After a few moments the solution takes on a rose-red color, showing that the acid of the urine has been neutralized. One now adds 10 c.c. of 10 per cent. sodium phosphate, allows the mixture to stand from two to three hours, and then filters. 15 c.c. of this filtrate are neutralized with one-fourth normal sulphuric acid, and after the addition of 5 c.c. of neutralized formol the resulting acidity is estimated, using one-tenth normal sodium hydroxide, 1 c.c. of which equals 0.0014 gm. of amino-acid nitrogen. Increased amino-acid excretion occurs in insufficient amino-acid destruction on the part of the liver, in cases where pathological destruction of proteids is going on, and third, in conditions of acidosis, whether diabetic or of another nature. Of 40 cases of hepatic disease, all cases which showed a marked injury to the tissues showed an equally marked increase of amino-acid in the urine. Normal values occur in uncomplicated gall-stones and catarrhal jaundice. The same is true in the cases of early Laennec's cirrhosis, but in the later stages of the disease the excretion is increased. Abnormally high values also occur in fatty degeneration, cases of primary tumor, cirrhosis secondary to cardiac disease, and in cases of phosphorus and chloroform poisoning. In cases of marked diabetic acidosis, values of from 0.92 to 3.04 gm. of amino-acid nitrogen per day were found, these values representing 8.4 to 18.4 of the total nitrogen output. In a number of diseases of the gastro-intestinl tract, in gout and chronic rheumatism, normal values were found. In those acute and chronic diseases which are accompanied by an abnormal breaking down of protein tissue, such as occur in the late stages of typhoid, in the crisis of pneumonia and during the absorption of pleuritic and other exudates, in leukemia, etc., constant increased

amino-acid excretion was observed in the urine. As a functional test, designed to show the inability of the liver to perform its normal amino-acid decomposition, Lobbe and Bith recommend the administration of 20 gm. of pepton while the patient is on a simple milk diet. If under these conditions an increased amino-acid excretion is observed, in all probability this indicates an affection of the liver.

Sulphemoglobinemia.—R. L. M. WALLIS (*Quart. Jour. of Med.*, vii 73 to 91) gives an historical review of the literature on the subject of sulphemoglobinemia, bringing together a total of 5 cases, including 3 observed personally. He further presents a clear *resume* of the chemistry and spectroscopic tests for this substance in the blood. All the cases present a fairly characteristic clinical picture dominated by the presence of extreme cyanosis, weakness, headache, and constipation, without dyspnea, heart disease, or alteration in the red-blood count. The diagnosis may be easily made by the spectroscopic examination of the blood or even of the lobe of the ear. The urine in these cases is apt to be extremely dark. As a special finding the author notes the occurrence in the saliva of nitrite-forming bacteria, which have been readily secured in pure culture and are easily grown on most media at a temperature of about 25° C. These bacteria apparently produce their nitrites from the amino-acids of the blood and impart to the latter a reducing substance, the exact nature of which is not yet known though it is probably a hydroxylamine derivative. This substance, according to the author, caused a partial reduction of oxyhemoglobin, which is subsequently converted into sulphemoglobin by the hydrogen sulphide arising from the intestinal tract. The author made some attempts at vaccine therapy, using the nitrite bacillus, but with doubtful results. Careful regulation of the intestinal movements has some influence upon the condition, but like oxygen inhalations only of a transient nature.

Complement-deviation in Graves' Disease.—ROSEO (*Il Policlinico*, xx, 1249 to 1251). In a previous communication Roseo showed that the sera of 4 out of 5 cases of typical exophthalmic goitre gave complete complement fixation with each of two aqueous antigens made from thyroid tissue removed at operation. The sera from cases of the so-called "formes frustes" gave negative reactions with the same antigens, while the sera from 13 normal people and those from 5 cases of lues, which were confirmed by the Wassermann reaction, also gave negative results. Since reporting this first series in 1912 the author has continued the test, running the sera parallel with the Wassermann reaction in order to see if the above fixation is a specific phenomenon or one due to some factors common to both goitre and lues. He has secured complete fixation in 4 cases of true Graves' disease and negative results in 3 mild cases and in 2 patients suffering with thyroid adenomas. In only 1 of the above cases was there a positive Wassermann, but in this instance a previous luetic infection was admitted. These reports are rather in accord with the work reported by Papazoula, who secured 58 positive reactions out of 60 cases investigated. Papazoula also secured negative results when testing control sera with the Basedow antigens. Roseo further reports the examination

of sera of four patients after removal of the thyroid gland. In two of these there was marked postoperative clinical improvement, and the test became negative within fifteen to thirty days after operation. The author advances some hypotheses as to the nature of the reaction, but admits that the evidence at present is far too meager to permit of any definite conclusions.

SURGERY

UNDER THE CHARGE OF

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Valve Formation in the Urinary Bladder for the Escape of Ascitic Fluid.—Rosenstein (*Zentralbl. f. Chir.*, 1914, xli, 373) conceived and put into practice the idea of permitting the ascites, due to liver cirrhosis, to escape into the urinary bladder. A woman, aged sixty-two years, suffered from liver cirrhosis and ascites since 1911. Rosenstein made an anastomosis between the portal vein and the inferior cava, *i. e.*, an Eck fistula. Unfortunately the success was only temporary. Later he did a Talma operation (suturing the spleen and great omentum to the abdominal wall and painting the surface of the liver with tincture of iodine), but this was also unsuccessful. In June, 1913, he did the following operation: The abdomen was opened freely and the whole peritoneal covered portion of the bladder exposed. He then drew a portion of the summit of the bladder through a silver ring, 3 cm. in diameter, cut the apex of this portion of the bladder with a scissors, and turned the margins over the ring all around so that the serosa was applied to serosa and fixed it in this position by silk sutures. This gave a free communication between the bladder and peritoneal cavity. He then excised a strip of the serosa and muscularis of the bladder wall all around below the ring and silk sutures, leaving only the mucosa. The upper and lower margins of this raw surface were sutured together, muscularis to muscularis and serosa to serosa. This forced the mucosa layer inward in the form of a circular double layer which, when the bladder was allowed to drop into place, acted as a valve to prevent the escape of urine into the peritoneal cavity. But it permitted the ascitic fluid to make its way into the bladder. The operation also provided against leaving any sutures in the mucosa, which is important in all bladder operations. The abdominal wound was closed, primary healing occurred, and after a short time the patient left her

bed. The ascitic fluid passed out with the urine, and the cystoscope showed that the valve functionated perfectly. The cure was not complete, as the ascitic fluid had to be withdrawn by puncture about every eight weeks, whereas before the first operation it was done about every eight days.

Thirteen Years' Experience with Pyloroplasty.—FINNEY and FRIEDENWALD (*Surg. Gyn. and Obst.*, 1914, xviii, 273) present their results with this operation, which Finney introduced in 1902, and a discussion of its advantages and disadvantages. The records of 100 cases, in which the operation was done, were studied. Of the 100 cases, the final results in 17 are unknown, while 5 died soon after operation, leaving 78 cases, in which the average percentage of favorable satisfactory recoveries was 93.8 per cent., the later deaths, 5 per cent., or favorable results 88.8 per cent. The operation has its greatest indication in the relief of pyloric stenosis, due to chronic ulcers, situated at or near the pylorus, and on either side of it or resulting from cicatricial contraction following the healing of such ulcers. It is often a useful procedure in cases of hemorrhage due to gastric ulcers on the lesser curvature or to duodenal ulcers which cannot be controlled medically, and which threaten the life of the patient, as well as in the chronic dyspepsias due to ulcers which have not been relieved by medical treatment. The operation has certain advantages over gastro-enterostomy and few of its disadvantages. Such objections as are advanced against the operation, *e. g.*, its inapplicability in the presence of active and bleeding ulcers, and also because of the fact that the new opening is not at its lowest point, taking advantage of gravity, are, according to their experience, more fanciful than real, since the operation has frequently been performed under these circumstances with most gratifying results. The interesting experimental work of Cannon and Blake and others supports this contention. The only contra-indications to the operation are inability to mobilize the duodenum when adhesions are too dense, and thickening and infiltration about the pylorus due to hypertrophic forms of ulceration. These are rare, however. In atony or gastroptosis with slight motor insufficiency such as observed in the water-trap stomach, or in nervous dyspepsia, *i. e.*, in gastric disturbances not dependent upon organic disease, this operation is contra-indicated. The special advantages lie in its affording the opportunity to excise all ulcers in the anterior walls of the stomach or duodenum after direct inspection of the part affected; also the application of treatment to ulcers situated in the posterior walls. It does not greatly disturb the normal relation between the stomach and intestines, as is the case in other operations. From their experience the immediate as well as the final results are most encouraging, while in some instances partial gastrectomy or gastro-enterostomy is undoubtedly the operation of choice; nevertheless, on account of its simplicity and satisfactory end results, they believe that pyloroplasty will continue to retain its position as a safe and useful procedure.

The Direct Implantation of Nerves into Muscles.—HEINEKE (*Zentralbl. f. Chir.*, 1914, xli, 465) experimented on the hind legs of rabbits. The two branches of the sciatic nerve, the internal and the external

popliteal nerves, were exposed in the thigh and a piece of the internal, 1 to 2 cm. long, was excised. The posterior muscles of the leg were thus paralyzed completely. The external popliteal or peroneal nerve was then followed outward and downward and divided below the head of the fibula. Finally a small channel was made through the gastrocnemius in a suitable place by a blunt instrument. The proximal end of the peroneal nerve was then passed through this channel and fixed in position by suturing over it a small muscle fold. Fourteen days later mild responses in the gastrocnemius were obtained by faradic and galvanic irritation of the peroneal nerve. After four weeks the whole prominence of the gastrocnemius reacted with strong contractions. After eight weeks the strength and extent of the contractions could not be distinguished from the normal, and not only did the muscle contract in which the nerve was implanted, but the neighboring muscles of the flexor group as well. At this time the muscles, which in the beginning were wasted and yellow, had recovered completely their normal color and consistency. Heineke has also shown that a muscle deprived of its nerve supply for twenty-one days, from the implantation of a sound nerve, can recover its function.

A New Method for the After-treatment of Prostatectomy.—Van Bisselick (*Zentralbl. f. Chir.*, 1914, xli, 503) says that the method makes use of a permanent catheter for a few days after the operation, so that only a small opening in the bladder wall is necessary through which a tampon is brought out. After the removal of the prostate in the usual way the wound and, if the hemorrhage is severe, the whole bladder are tamponned with gauze. The catheter, which was used before the operation to irrigate and empty the bladder, is left in position in the bladder, The greater part of the bladder wound is closed in two layers, catgut for the mucous membrane and silk for the outer layer. The part of the bladder wound remaining open is enclosed with a purse-string suture of catgut, which is passed from the outer side to the muscularis, but is not left long. The space of Retzius is tamponed and the abdominal wound is closed around the bladder tampon. Usually this is removed in twenty-four hours. The bladder is then washed out from above and below and the bladder wound is closed by inversion of its edges and tying the purse-string suture. A tampon down to the closed bladder wound will provide for the escape of any urine that will escape later. The bladder is washed out every two hours and the catheter changed every day. This continues for three or four days. Then it is left out at night for seven or eight days. After that the patient can urinate spontaneously at night. Six of the nine cases operated on in this way urinated spontaneously within fourteen days. The three remaining cases had cancer of the bladder.

Bimanual Examination of the Prostate.—Haberland (*Zentralbl. f. Chir.*, 1914, xli, 675) finds the bimanual method of examination very satisfactory. Since the anterior surface of the prostate lies behind the lower portion of the symphisis pubis, the finger reaches it when introduced into the rectum only 4 to 6 cm. from the external sphincter, while the finger of the other hand can be pressed downward against

the empty bladder and abdominal wall and thus against the prostate as in examining the uterus in the female. Even with a thick, tense abdominal wall, the method will rarely fail. Haberland has proven the correctness of his diagnosis by prostatectomy. By practice, one can determine the size and form of the seminal vesicles and vasa deferentia. By this method, the diagnosis can be made between vesical calculus and hypertrophied prostate. Only in isolated cases will it be necessary to invoke the aid of the *x*-rays, for more certainty in the differential diagnosis between these two conditions. The patient lies on his back with the knees drawn up and breathing through his mouth. The bladder is first completely emptied, voluntarily or by catheter. Fecal masses in the rectum do not disturb the examination.

THERAPEUTICS

UNDER THE CHARGE OF

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The Emetin Treatment of Amebic Dysentery.—YEOMAN (*New York Med. Jour.*, 1914, xcix, 327) reports 7 cases of amebic dysentery treated by subcutaneous injections of emetin hydrochloride. The disease varied in duration before treatment with emetin from six months to fourteen years. Other forms of treatment, including ipecac in 4 cases, had been employed in all the patients, with temporary benefit only, 5 patients were cured clinically, 2 were greatly improved, and none died. One of the "cured" cases recurred five months later. The average dose of emetin hydrochloride is one-half grain dissolved in 10 to 15 minims of salt solution and injected subcutaneously in the region over the deltoid. The remedy should be given until the symptoms disappear, and then the administration of emetin should be discontinued, for an excessive amount of emetin frequently produces marked bowel irritation. Yeoman believes emetin is specific for amebic dysentery in the same sense that quinine is specific for malaria or salvarsan for syphilis. When it is used early in the disease, cure should be prompt and permanent in all cases. Naturally when the amebæ have invaded the tissues deeply and are widely disseminated, cure may be permanent or clinical only. After weeks, months, or years encysted amebæ may reappear in an active vegetative form, accompanied by all the symptoms of an acute attack. Hence amebic patients should be kept under prolonged observation, and at the first signs of recurrence a course of emetin should be given. Because of the extensive destruction of the mucosa and the secondary infection of the ulcers, mucus, pus and blood in diminishing quantities may continue to be evacuated for sometime after all amebæ have disappeared from the stools. Irrigations and topical applications through the proctoscope will materially hasten the process of tissue repair.

The Magnesium Treatment of Tetanus.—STADLER (*Berlin. klin. Woch.*, 1914, li, 15 and 109), reviews the evidence of many observers on both the magnesium and phenol treatment of tetanus, and includes tabulated results of the different methods of treating tetanus. The results of the magnesium treatment compare very unfavorably with the results of Bacelli's method in the hands of the Italians. French, English, and Russian surgeons have also obtained excellent results with Bacelli's method, which is in contrast with the unfavorable results reported by German surgeons. Stadler says that at the present time it is impossible to judge of the relative advantages of the two methods. In general, he believes that phenol is more efficacious than magnesium, but if magnesium is given subcutaneously instead of intraspinally the difference is not so great. He is of the opinion that both methods add to the percentage of cures, but especially when they are combined with the serum treatment. He emphasizes the fact that more experimental and clinical evidence is necessary in order to determine which is superior. The article is very comprehensive, and reviews the literature of the subject in great detail.

Treatment of Tetanus by the "Rational" Method of Ashhurst and John.—BREM (*Jour. Amer. Med. Assoc.*, 1914, lxii, 191) quotes Ashhurst and John, who believe that the rational use of tetanus antitoxin consists in the intraneural injection of antitoxin; the intraspinal injection; the intravenous injection, and the infiltration of the tissues about the site of the injury. The quantity used should be very much greater than the quantity that has usually been given heretofore by the subcutaneous route. They have administered as much as 224,000 units during a period of three days. These authors feel that the outlook for patients with tetanus is much brighter since the development of this method of administering antitoxin, and that the old view, that antitoxin is of no avail after the symptoms of tetanus have developed must be abandoned. Brem reports a case of tetanus, treated along the lines suggested by Ashhurst and John, with very rapid recovery. This patient received a total of 98,000 units of antitoxin.

Serum Therapy in Scarlet Fever.—MOOG (*Therap. Monatsheft*, 1914, xxviii, 37) reports 25 cases of scarlet fever treated by intravenous injections of normal serum. The results obtained were very similar to those obtained by other observers with the use of serum from scarlet fever convalescents. The most striking effect obtained was a critical drop in the temperature, which begins in two to four hours after the injection and reaches its maximum in from eleven to sixteen hours. In addition to this drop in temperature is a corresponding favorable influence upon the toxic symptoms. The best effects obtained were in the severe uncomplicated toxic cases. Septic complications of scarlet fever were not influenced by this method of treatment. The author believes that the benefit ascribed to antistreptococus serum in some cases to probably due to the effect of the serum alone. The injections should be made as early as possible in the course of the disease and not less than 80 or 100 c.c. of serum should be injected at one dose for children and 100 to 180 c.c. for adults.

Behring's Diphtheria Vaccine.—KISSLING (*Deutsch. med. Woch.*, 1913, xxxix, 2500), immunized 310 children following Behring's new method of combining the principles of both active and passive immunization. These children were exposed to an unusually virulent epidemic of diphtheria. Of 111 children who received two prophylactic injections none contracted diphtheria; of the remaining 119 cases receiving only a single injection 8 developed diphtheria. These 8 children were convalescing from scarlet fever and developed the disease in a mild form. Since the process of immunization requires several days it is possible that the disease developed in these cases before the time required to develop the immunity against the disease had elapsed. Kissling is convinced of the efficacy of this new method of immunization, and believes that it is far superior to the *older* method.

Some Theoretical Considerations Regarding Splenectomy in Pernicious Anemia.—EPPINGER (*Berlin. klin. Woch.*, 1913, I, 2409) advances a theory to explain the beneficial effect of splenectomy in pernicious anemia. He believes that the red-blood cells are destroyed in abnormal numbers in the spleen in pernicious anemia due to anatomical changes in the bloodvessels of the spleen. These changes allow large numbers of red-blood cells to enter the splenic pulp, where they are destroyed; the condition is essentially that of the pernicious anemia following hemorrhage, the patient bleeding into his own spleen. Eppinger found certain histological changes in the spleens of seven patients he removed that seem to support this view. He suggests that where the spleen cannot be removed, possibly ligature of the splenic artery might answer the same purpose. Eppinger also calls attention to the presence of "blood-lymph-nodes," that often are found in great numbers in cases of pernicious anemia. They seem to be similar to splenic tissue in their structure, and he suggests that when splenectomy does not benefit in pernicious anemia that these blood-lymph-nodes may be able to carry on the blood-destroying action of the spleen.

PEDIATRICS

UNDER THE CHARGE OF

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Hemorrhagic Disease of the Newborn and Direct Transfusion of Blood.—V. D. LESPINASSE (*Jour. Amer. Med. Assoc.*, 1914, lxii, 1866) gives as the chief causes of hemorrhagic disease in the newborn, syphilis, infection, hypoplasia of the coagulating elements of the blood, and asphyxia. Obstetrical complications and chloroform are of minor importance. According to Holt, syphilis is a causative factor in only 2 per cent. to 6 per cent. of the cases. The chief pathological lesions are the same as the clinical lesions, namely, hemorrhage and its conse-

quent anemia. The symptomatology is striking. Occasionally premonitory signs, such as restlessness, refusal to nurse, and slight elevation of temperature, are present. The chief symptom is spontaneous hemorrhage, and its site may be from the intestines, stomach, mouth, nose, ecchymoses of skin, pressure points of body, meninges, genito-urinary tract, and eyes. Progressive pallor of the skin, gradual drying up of the tissues, weakening pulse, coma, and death follow a persistent hemorrhage. A black, tar-colored mass, with a pink fringe, seen in the stool, indicates hemorrhage in the gastro-intestinal tract. The treatment is the same whether the case is one of hemorrhagic disease of the newborn, Winkel's disease, Buhl's disease, jaundice with hemorrhage or hemophilia. The hemorrhage usually appears from the second to the fifth day of life; the earlier the onset the more grave the prognosis. In half the fatal cases death occurs suddenly within twenty-four hours or less. This is especially true in hemorrhages from the gastro-intestinal tract. The shortest clinical course observed by Lespinasse was four hours. A hemorrhage of one ounce in a newborn baby is equivalent to one quart in an adult. The three indications in the treatment are to stop the bleeding, replace the lost blood, and overcome the infection. Transfusion of live non-clotted blood meets all these indications in an ideal manner. This method will cure in practically every case, and it is never too late to transfuse if there is still the slightest auricular beat. Bowel cases should be transfused early. In Lespinasse's series of fourteen cases there have been no deaths from hemorrhage. The cessation of bleeding and the improvement in the general condition are simultaneous with the transfusion.

Juvenile Paresis and Salvarsanized Serum.—C. EUGENE RIGGS (*Jour. Amer. Med. Assoc.*, 1914, lxii, 1888) reports a case of juvenile paresis treated by the intraspinal injection of salvarsanized serum. The symptoms of juvenile paresis differ in no way, clinically or pathologically, from those of the generally recognized type. In either congenital or acquired syphilis the symptoms are due to the action of the Spirocheta pallida on the brain cortex. About one-half the cases develop after adolescence. It may occur in the very young, showing itself in mental retardation or feeble-mindedness. Fennell claims that 5 per cent. of imbecile children are congenital general paretics. Optic atrophy is an early symptom. Riggs reports the case of a boy, aged eight years, whose father had syphilis and gave a positive Wassermann reaction. Of the three other children in the family one gave a positive and two gave a negative reaction. The mental deterioration began in the boy's fourth year. At eight years the boy showed Argyll-Robertson pupils, exaggerated knee-jerks, ankle-clonus, and Babinski reflex in both feet, and marked Rombergism. There were no signs of congenital syphilis. The boy received eight intravenous injections of 0.25 gm. salvarsan followed next day by an intraspinal injection of 30 c.c. of a 40 per cent. solution of salvarsanized serum. The result was a return to normal pressure in the spinal fluid and a less positive blood-serum reaction. The other serobiological tests remained the same. But clinically, a marked improvement was noted, as the boy again fed himself, his vacuous expression disappeared, he became brighter mentally, and his gait improved.

OBSTETRICS

UNDER THE CHARGE OF

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Inversion of the Uterus.—BECKMANN (*Zent. f. Gyn.*, 1914, No. 18) reports the case of a woman in very weak condition, through repeated hemorrhage from an inverted uterus. This resulted from spontaneous birth under the care of a midwife. The patient was admitted to hospital, the abdomen opened by vaginal incision, the posterior wall of the uterus incised to the fundus, and the uterus reinverted. The tissues were then closed by suture and the uterus replaced in the abdominal cavity. The closure of the posterior vaginal wall completed the operation. The patient's recovery was complicated by infection without symptoms of peritonitis. The posterior cul-de-sac was opened and seropurlent fluid, containing abundant streptococci, was discharged. A drainage tube was inserted and the cavity of the uterus disinfected with tincture of iodin. The patient died of septic infection two days later. The second patient was subjected to colpeurysis for seven days without result. Operation was then undertaken and the uterus replaced. Infection followed and drainage and the use of iodin were then employed. The patient made a tedious recovery. These cases emphasize the danger of infection and seriously raise the question whether in cases where infection has persisted long it is not better to extirpate the uterus.

Clinical Manifestations of Congenital Syphilis.—ARMSTRONG (*British Med. Jour.*, May 2, 1914) believes from clinical observation that while cases of congenital syphilis are becoming more frequent the severity of the disease is decreasing. Necrosis of the bones does not appear so often, but syphilitic disease of the nervous system, congenital in infants, seems to be on the increase. Improvement in diagnosis results in recognizing many cases which otherwise would have passed unnoticed. While the Wassermann reaction is reliable in the majority of cases the luetin test is better. In pregnancy the Wassermann reaction from the mother's blood is valuable and suggestive. In marasmic children the Wassermann test is often negative. Ten per cent. of pregnancies in syphilitic women result in the death of offspring before the end of the first year of life. The percentage of abortions is very large. In some cases repeated abortion is followed by the birth of a monstrosity. With the syphilitic rash may be confused pemphigus of the newborn. A true pemphigus is the result of a streptococcus infection of the skin. A syphilitic eruption with blebs is rarely found in newborn infants; when present it is on the palms and soles and is soon followed by the raw-ham color. Pemphigus occurs after birth and is not limited to the palms and soles. The syphilitic child is badly nourished; the infant with pemphigus may be well nourished. Eczema

affecting the scalp may be confused with congenital syphilis. In the former the eruption is scaly, greasy, and yellow on the scalp and folds in the face and behind the ears. When this occurs about the nates and is complicated with lack of cleanliness, inflammation and oozing may develop, which resembles syphilis. Gangrene occurring in a newborn child may be the result of syphilis, and a therapeutic test would clear up the diagnosis. After the first few years of life, children born syphilitic show the disease most often in laryngitis and warts. The latter are easily seen and cured. The laryngitis is chronic with acute attacks, and syphilis may not be suspected as a cause. Here a therapeutic test makes a diagnosis possible. Congenital syphilis may cause a discharge of blood in the urine. In these cases edema is usually a prominent symptom, and if autopsy is obtained the kidneys, on microscopic examination, show characteristic changes. In diseases of the nervous system, infants born with marked evidence of syphilis usually die early, those apparently healthy developing defects at the time of the second dentition or puberty and often develop paralysis. In other cases mental deficiency, imbecility, and idiocy may be present without physical sign of syphilis. In these the Wassermann reaction make the diagnosis. Meningitis in these cases is often basal, and while the child may not die it is usually permanently damaged. Syphilitic infants often become hemiphlegic, and when this develops suddenly its occurrence is suspicious. Syphilitic children occasionally develop locomotor ataxia which is usually incurable.

Cesarean Section for Heart Disease.—BARRIS (*Jour. of Obs. and Gyn. British Empire*, April, 1914) reports the case of a multipara, with a history of rheumatism, who passed through a tenth labor without signs of cardiac failure. When admitted to the maternity department of St. Bartholomew's Hospital she was in a critical condition, the urine albuminous, the heart greatly dilated, with double aortic and mitral disease. An electrocardiagram showed extensive disease of the heart muscle. Although the child was not viable the mother's condition was so grave that pregnancy must immediately be ended. It seemed also best to sterilize the patient. Accordingly, stovain with dextrose dissolved in sterilized water was injected between the third and fourth lumbar vertebræ. A second injection was necessary, followed by full anesthesia. The patient's face was screened, so that she could not witness what was done. The operation was performed in the usual manner, and oxygen was administered and 1 c.c. pituitary extract. The patient felt no pain and blood-pressure, which at first was 240 mm. Hg., fell to 160. The pulse was from 90 to 55, then 75. Anesthesia lasted one hour, and a sandbag was placed on the abdomen to maintain intra-abdominal pressure. The uterus contracted well without hemorrhage, and the mother did well. Barris also has collected a report of a case done by Watts, under spinal anesthesia for mitral stenosis and kidney disease, at eight months pregnancy. The mother did well and the child was born alive. Wyatt operated at St. Thomas' Hospital under spinal anesthesia, tropococain with adrenalin, with delivery of a living child. The patient vomited during the operation. She died on the fifth day from cardiac failure. Stabb operated at Queen Charlotte's Hospital, using stovain and giving gas and

oxygen, a living child being born, which died nine days later from bronchopneumonia. The mother recovered. Under the conditions present this method seems clearly indicated.

Influence of Ectopic Pregnancy on the Uterus.—SAMPSON (*Surgery, Gyn., Obs.*, May, 1914), from an extensive study of the subject, finds that in early ectopic pregnancy the uterus increases in size by hyperemia of its muscle and thickening of its lining membrane. In the latter the changes are similar to those found in the decidua vera of early uterine pregnancy. The uterine wall shows arterial and venous hyperemia. The uterus contracts when the pregnant tube endeavors to expel its contents. These contractions lessen the arterial supply and damage the endometrium, causing outflow of blood. When tubal pregnancy ends the uterus undergoes involution: (1) by destroying recently developed tissue, and (2) by reconstructing new and normal tissue. The first takes place by free hemorrhage from the endometrium, with destruction of cells and filling of venous spaces. In the tube a similar process goes on, so that chorionic villi may remain in active condition in the tube indefinitely.

Retained Portions of Placenta; Their Significance and Management.—WINTER (*Monats. f. Geb. u. Gyn.*, 1914, Bd. 39, Hft. 5), contrary to much accepted belief, considers that retained portions of the placenta, in many cases, cause no disturbance whatever. He believes that symptoms developing in these cases were caused by local endometritis, or by infection at the placental site, developing in the conduct of labor. Instead of adding to the severity of infection in these cases, his observations led him to think that retained portions of placenta may actually make infection less severe. He is against the common practice of, in all cases where fever occurs, exploring the uterus for retained placental fragments. Under antiseptic precautions this can be done without causing fever in one-third of the cases; while in from one-half to two-thirds, reaction more or less severe occurs, and in 7 to 9 per cent. death follows. Infection by hemolytic streptococci seems to be the cause of the fatal result. The spontaneous expulsion of portions of placenta is without danger, and usually terminates fever which may be present. Infection in these cases does not enter the connective tissue of the uterus nor its blood-current, and hence recovery is rapid. So far as treatment is concerned he would not interfere with the uterus, because a portion of placenta was retained, unless hemorrhage occurred. When at the moment of labor the placenta does not completely come away, retained portions should be immediately removed. During the puerperal period, in cases without fever, where it is known that a portion of placenta is retained, this should be removed. When fever is present in the puerperal period, accompanied by hemorrhage and retention of a portion of placenta, the placental fragments must be removed. When there is no hemorrhage, but where placental polyp is present in the cervix or extending into the vagina, one should wait for spontaneous expulsion, helping it by the administration of ergot. Should this not succeed, bacteriological examination of the lochia should be made, and if the less virulent ferments or bacteria are present the uterus should be immediately cleared out. If virulent bacteria, as

streptococci are present, this should not be done, and one should wait for spontaneous expulsion of fragments or until pathogenic bacteria have disappeared. When it is evident that the peritoneum, parametria or adnexa are involved, active interference is contra-indicated. Active hemorrhage only would be a cause for operation. When it is decided to remove placental fragments, it should be done by the finger and not by a curette.

GYNECOLOGY

UNDER THE CHARGE OF

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Ovarian Transplantation.—The question of reimplanting into some portion of the patient's body one or both ovaries, or a portion of them, in order to prevent the various nervous sequelæ which so often follow an abrupt, surgical menopause, has interested surgeons for many years. This procedure comes into consideration of course only in cases in which, owing to the presence of advanced inflammatory or other changes, a truly conservative type of operation is impossible, and both ovaries must be removed. It having been pretty definitely proven that no type of heteroplastic transplantation offers the slightest hope of success, attention in recent years has been directed toward the reimplantation, as has been said, of the patient's own ovarian tissue, after freeing this from surrounding diseased structures. The chief experimenters along these lines at present are the French surgeons, especially TUFFIER, but a recent report from one of the French clinics by DE ROUVILLE (*Arch. mens. d'obst. et de gyn.*, 1914, iii, 161) is decidedly discouraging, and does much to justify the marked skeptism with which is the procedure is viewed by the majority of American operators. De Rouville reports the results in nine cases of autoplastic ovarian grafting, performed in conjunction with operations for various inflammatory conditions of the genital organs. In each case one or both ovaries was implanted beneath the skin of the abdominal wall, just to one side of the line of incision. *Anatomic Results:* So far as could be determined from subsequent abdominal palpation, the implanted ovary or ovaries underwent complete disappearance in four cases, and showed very marked atrophy in three others, the periods of observation varying from five to thirty-two months. In one case, the ovary remained apparently the same size at the end of seventeen months, and in the ninth both ovaries had been implanted, and both increased in size. In this instance, it became necessary after a year and a half to extirpate the ovaries, as they had become extremely painful, and a condition of excessive menorrhagia and metrorrhagia had developed. After removal of the ovaries, these symptoms entirely disappeared, and the patient regained good health. Microscopic examination showed some fibrous and hyaline changes in the stroma, numerous developing and

cystic follicles, and a well-developed but degenerating corpus luteum. The tissue appeared incontestably to have been living and functionating, but showed distinctly beginning degenerative changes. *Functional Results:* In five cases the implanted ovaries became at times (usually, but not always, immediately preceding menstruation) congested and painful; in the other four patients no such disturbances were complained of. In two instances, a hysterectomy was performed, and subsequent menstruation could not therefore be expected; in six of the remaining seven cases some evidence of menstruation became manifest, but in only one patient was a fairly normal menstrual life established. In all the others, menstruation was distinctly abnormal, being either irregular from the start, or regular for a short time, then becoming irregular, scanty, and finally ceasing, or in one instance, as already mentioned, giving place to excessive hemorrhages. To summarize; De Rouville was able to see a real permanent advantage to the patient from the graft in but one instance; in a second there was a definite benefit for a short time only, and in a third there was some questionable benefit. The others were not in the least improved, and in some cases harm was apparently done—at least disagreeable sequelæ followed. De Rouville is therefore decidedly opposed to the use of grafts as a routine measure, and thinks that with our present technique the most that can be expected from them is the production of a gradual instead of an abrupt loss of the ovarian secretion.

Ovarian Secretion and Uterine Fibroids.—An attempt has been made by MAYER and SCHNEIDER (*Münch. med. Woch.*, 1914, li, 1042) to determine by means of the Abderhalden reaction whether there is any functional disturbance in the ovaries of patients suffering from uterine fibroids. While their investigations as reported are rather few in number, and by no means conclusive, they represent a somewhat new point of attack upon this much discussed subject, and present therefore some points of interest. The sera of thirty myoma patients were tested out by Abderhalden's dialysis method against extracts of their own ovaries (removed at operation), and against ovaries from other myoma patients, from carcinoma patients, pregnant women, and, so far as possible, women suffering with no genital disease. The ovaries from the carcinoma cases, and other extra-genital conditions, gave in every instance a negative reaction; in about 50 per cent. of the tests with ovaries from another myoma patient the reaction was positive, while in a considerable majority of those with the myoma patient's *own* ovaries a positive result was obtained. It has been shown by Abderhalden, as well as others, that the reaction is positive with a specific organ only when either the internal secretion of that organ is altered from the normal, or when anatomic changes are present in it amounting to practical destruction. Since we know from histological studies that the latter is not the case with regard to ovaries associated with uterine myomas, the causes for the positive reaction in so many instances must lie, Mayer and Schneider think, in a disturbance of the ovarian secretion, or, as they term it, a "dysfunction" of the ovaries. They believe that this is primary, and the development of the uterine tumors secondary, not *vice versa*. They believe also that the sterility, which so often accompanies uterine fibroids, is neither the result nor

a cause of the tumors, but that it likewise is a result of the disturbed ovarian function, as is the marked delay and irregularity in the onset of the menopause, which is often seen in these cases.

Dissection of the Ureter in the Radical Operation for Uterine Carcinoma.—MAYER (*Zeitschr. f. Geb. u. Gyn.*, 1914, lxxv, 399) says that while in many cases the ureter is easily found by the process of separating from above the layers of the broad ligament, in occasional instances this becomes very difficult, especially in the presence of senile or inflamed tissues. Moreover, at times numerous branching veins are present throughout the whole of the broad ligament, and give rise to exceedingly annoying hemorrhage as they are ruptured in separating the layers. In such cases, he has found the following slight modification of the usual technique of great service: The ureter can almost always be distinctly seen shining through its peritoneal covering in the higher portion of the posterior pelvic wall, or at the point where it crosses the great vessels. If the operator, after severing the round ligament and adnexa, draws the uterus forcibly forward and to the opposite side, before any dissection has been done to disturb the natural relations, it is always easy to trace the ureter down by sight to its point of entrance into the parametrium. If a small longitudinal incision be made in the peritoneum at this point, immediately over the ureter, the latter will be exposed without having separated any of the tissues of the broad ligament, and therefore without the production of any hemorrhage. If now the ureter is lifted by means of a long blunt hook, or similar instrument, to one side or the other, the entire posterior layer of the broad ligament can be cut through low down, exposing the uterine artery and ureter in their entire course through the ligament, without the necessity for any blunt dissection of tissue. By this means, it is possible to remove a larger amount of paremetrium than by the usual methods, and the uterine artery is easily exposed for ligation, without any danger to the ureter.

Action of Ovarian Lipoids upon the Genital System.—An interesting report has recently been made by ISCOVESCO (*Rev. de gyn. et de chir., abdom.*, 1914, xxii, 161) upon some experimental and clinical studies of certain lipoids obtained from human ovaries. As Iscovesco points out, every gland of internal secretion throws into the circulation a number of different lipoidal substances, one of which appears to have the specific action of stimulating the secretory activity of the gland itself. Fresh human ovary was found to contain about 3 per cent. by weight of total lipoids; extracting these by means of ether, acetone, chloroform, alcohol, etc., Iscovesco was able to distinguish five main groups, of which the fifth, or alcohol-soluble group is much the most important. By further solution and precipitation, this group can be subdivided into several different constituents, one of which, called by Iscovesco VDc, appears to exert a marked stimulant acting upon the ovary and whole genital system. It is a yellowish, wax-like substance; which for experimental and clinical use was made up in a 2 per cent. solution in oil. This solution may be injected hypodermically or intraperitoneally into laboratory animals, without any signs of irritation or infection. A series of young rabbits injected daily, or at inter-

vals of a few days, for a considerable period of time, all showed when killed and autopsied an enlargement of the ovaries and uterus to two or three times the size of these organs in controls; very young animals, in whom the injections were started at the sixth week and continued until the fifteenth week, showed by that time genital organs exceeding in size and weight those of adult animals. Practically no effect was produced in any of the experiments on any of the other organs, except the thyroid, which showed in the injected animals a slight increase in size; the effect here was much less, however, than in the genital tract. Iscovesco thinks the substance acts by direct stimulation of the genital centres in the central nervous system. For therapeutic purposes the same oily solution was given in 1 c.c. doses by deep injection into the gluteal muscles once daily, or four to six pills, each containing 2 cgm. of the lipoid, were given by mouth. The author reports astonishingly good results in the treatment of a number of cases of dysmenorrhea, amenorrhea due to ovarian hypofunction, and various nervous conditions in young girls, associated with irregular or painful menstruation, and probably having a basis in disturbed ovarian activity. Equally good results were obtained from the treatment of a number of patients suffering from the results of a natural or artificial menopause. Iscovesco does not think that the corpus luteum is responsible for the secretion of any substance essentially different from that elaborated by the entire ovary; if there is any difference, it is merely that the active substances are present in the corpus luteum in greater concentration. He has isolated from the corpus luteum a lipoid possessing identical chemical and physical characteristics with the one obtained from the ovary, and in a small number of animal experiments and therapeutic tests the results have been entirely similar.

DERMATOLOGY

UNDER THE CHARGE OF

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Disseminated Hematogenous Tuberculosis Verrucosa Cutis.—Bourgeois (*Dermatol. Zeitsch.*, Band xxi, Heft 1), who has made a most careful study of two cases of verrucose tuberculosis of the skin with multiple disseminated lesions, following, in the one instance measles, in the other scarlet fever, concludes that, besides the ordinary form which arises from local infection, there is a second, hematogenous in origin. The hematogenous form occurs chiefly in children with or without previous tuberculous symptoms, almost always after some one of the exanthemas, usually measles, much less frequently scarlet fever, and is not infrequently associated with other forms of cutaneous tuberculosis, such as the papulonecrotic tuberculide and lichen scrofulosorum. Clinically and histologically the hematogenous variety

agrees in every particular with that arising from local infection. While the lesions show a predilection for the extremities, the hands, feet, and elbows, they also occur on other parts, such as the nates, the trunk, the face, and genitalia.

The Significance of Cholesterin in Xanthoma.—SCHMIDT (*Dermatol. Zeitsch.*, Band xxi, Heft 2), employing the newer methods for the estimation of cholesterin in the blood and organs, has studied five cases of xanthoma, and found in all five patients a more or less considerable cholesterinemia, the cholesterin content being greatest in those in whom the clinical symptoms were most marked. The results of his investigation confirm completely the views of Pinkus and Pick that in patients with icterus and diabetes an infiltration of cholesterin fatty-acid esters takes place in the endothelial cells of the cutis and in the connective tissue, and that the deposition of these constitutes the chemical and histological characteristic of xanthoma. Schmidt believes that the cause of the xanthoma formation is to be sought in a constitutional anomaly in which an increase of cholesterin in the blood appears.

Dermatitis Papillaris Capillitii (Kaposis); Acne Keloid.—ADAMSON (*British Jour. Dermat.*, March, 1914), as the result of a recent study of four cases of this interesting affection, inclines to support the view of Kaposi that it is a chronic inflammation with the formation of new connective tissue which leads by pressure to atrophy of the glands and follicles. He regards friction by the edge of the collar as an etiological factor, and thinks a combined microbic and traumatic origin likely. He does not believe the acne bacillus nor the Staphylococcus pyogenes responsible for the affection, which in his opinion is not related to acne nor sycosis; nor is it true keloid. As to the treatment the author believes most success is obtained with the *x*-rays, using large and repeated doses.

Epidemic Alopecia Areata.—DAVIS (*British Jour. Dermat.*, June, 1914) reports an extensive epidemic of an affection resembling alopecia areata, occurring in an orphanage containing about 300 children, all of them girls. The first case was observed in March, 1913, and at the end of June there were no less than 174 cases. Daily washing with methylated spirit and soap and the application of ointments of β-naphtol and sulphur soon brought the diseases under control. A year later there was a new but less extensive outbreak which speedily yielded to treatment, which consisted this time in painting the patches with liniment of iodin. The patches were more like those of ringworm than ordinary alopecia areata, containing numerous stumps of hairs, but no fungus could be found. Although reporting the epidemic as alopecia areata, the author thinks it questionable whether the disease is properly so described.

Lichenoid Trichophytosis.—GUTH (*Archiv. f. Dermat. und Syph.*, Band cxviii, Heft 3), under the name lichenoid trichophytosis, reports fifteen cases of a disseminated or grouped lichenoid, occasionally psoriasiform eruption, which he has thus far observed only in deep

trichophytosis, especially in kerion of children. He regards the eruption as the expression of the trichophytin hypersensitiveness which appears in deep trichophytosis as an immunity phenomenon. By the application of trichophytin or the trichophyton to specifically hypersensitive skins analogous changes may be produced. The pathogensis of the spontaneous exanthem is not yet explained.

Fungus Affections of the Hands and Feet.—KAUFMANN-WOLF (*Dermatol. Zeitsch.*, Band xxi, Heft 5), under the above title, reports twenty-five cases of eruptive disease situated on the hands and feet, resembling at times dysidrosis at others eczema, in which various fungi were demonstrable. In 17 of these cases the trichophyton was present; in the remainder various other fungi were found. The author concludes that fungous affections of the hands and feet appear frequently under the picture of dysidrosis or of eczema. The chief symptom is deep-seated, grouped vesicles, which are inclined to suppuration and seldom ooze. The vesicles always lie within the epidermis, and, notwithstanding the absence of recognizable fungous elements in their contents, are infectious, as is shown by culture. The fungus is found in the uppermost layers of the epidermis.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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The Diagnosis between Exudates and Transudates.—MAURICE VILLARET (*Jour. de Physiol. et de Path. générale*, May 15, xv, No. 3) publishes two articles dealing with the methods at his disposal for distinguishing exudates from transudates. In the beginning he deals with the various reactions with which we are already familiar. The Rivalta, dating from 1895, consists in the use of distilled water faintly acidulated with acetic acid into which is gently dropped one drop of the fluid to be tested. In the case of a positive reaction, such as is given by an exudate, the drop descends, slowly becoming turbid, and finally bluish-white. As to the explanation of the reaction, Villaret favors the view of Patein, that the reaction is due to a specific albumin, acetoglobulin. It must be admitted that the subject has been widely debated without any fixity of opinion being as yet reached. The reaction of Gangi consists in taking from 3 to 4 c.c. of hydrochloric acid in a test-tube, and laying on top of it, carefully, 4 or 5 c.c. of the fluid to be tested and leaving it for some hours. If the reaction is positive, as occurs with an exudate, the upper fluid becomes turbid,

and there is a second ring of marked turbidity half way between the turbid disk lying next to the hydrochloric acid and the top of the fluid. Coagulation in the supernatant fluid is also an indication of positive result. The collargol test is made with a solution of collargol of the strength of 1 in 1000, freshly diluted to a strength of 1 in 25,000. Five test-tubes are filled two-thirds full of this solution, and into the first four are put 2, 5, 10, and 20 drops respectively, of the fluid to be examined. Mixed and carefully set aside away from the dust, they remain for twelve or fourteen hours before being examined. A negative result is shown by perfect limpidity of the solutions, and is to be expected in the presence of an exudate. Villaret considers that a positive reaction with the Rivalta and Gangi test with a negative collargol allows one definitely to conclude that one is dealing with an exudate; and on the other hand, a negative Rivalta and Gangi with a positive collargol test allows one to be certain that one is dealing with a transudate, and that these chemical tests suffice even in the absence of cellular examination, although the latter is highly desirable. In a second paper in which he deals with the examination of the cells in conjunction with the previously mentioned tests, Villaret divides ascitic fluid into three types. Of these the first is ascitic fluid occurring from mechanical causes such as one finds in blocking of the inferior vena cava, and in portal congestion. Endothelial cells are entirely or largely predominant, and the Rivalta and Gangi reactions are negative, and the collargol positive. The second division, ascites from inflammatory causes, may be characterized by lymphocytosis, as in tuberculous peritonitis, or by a mixed cellular picture where the endothelial cells demonstrate that portal hypotension is playing a part, as it might be expected to do in syphilis or cancer of the liver; or yet again by predominance of polynuclears, indicating that the ascites is infected to some degree. With such fluid the Rivalta and Gangi are positive, while the collargol reaction may be either positive or negative. From the two foregoing classes one may be able to distinguish mechanical ascites with secondary infection, in that the cellular picture becomes modified little by little, the polynuclears and lymphocytes progressively replacing endothelial cells. This change is preceded generally by a transformation of the Rivalta and Gangi test which from being negative, become positive: that is, from indicating a transudate, come to suggest an exudate. Finally, in far advanced cases, the transudate origin of the fluid can sometimes be determined by the persistence of the collargol positive reaction, which in the course of time becomes negative, showing that the infection has died out, or has at least been superseded by a mechanical transudate.

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